The upper limb in neuromuscular disorders

From basic function to daily life performance

Arjen Bergsma

DONDERS SERIES

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foar heit en mem

Contents

1 General introduction

1.1 Upper limb function

Our arms and hands are unique. Hardly any other living organism has such a pair of tools that can grasp, hold, move and manipulate objects like humans have. The arms, including the shoulder, upper arm, elbow, forearm and wrist connect the hands to our body. The arms enable us to position and rotate our hands in such a way that we can use them for whatever we want to do. Our arms and hands play a crucial role in the way we manifest and express ourselves. We use them not only to perform heavy labour but also to carry out gentle actions such as using a computer, playing piano or making friendly gestures to others. Our arms and hands are also important for supporting our communication. It is with good reason that the expression 'talking with one's hands' exists. The arm and hand together are also called the upper limb, or the upper extremity. These terms are often used in this thesis, when both the arm and hand are meant. Upper limb movements play a fundamental role in everyday life. Imagine you would have limited upper limb function, what a tremendous impact this would have on almost all areas of daily life.

1.2 Upper limb function in neuromuscular disorders

Several neuromuscular conditions can substantially impair the ability to use the arms and hands, due to muscle weakness or impaired muscle control, such as myopathies, neuropathies, mitochondrial disorders, motor neuron diseases and neuromuscular transmission diseases [1]. Different patterns exist with regards to the muscles that are involved in neuromuscular disorders (NMD). Some NMD mainly affect limb, axial and facial muscles, whereas in other types, respiratory, cardiac, and swallowing muscles may (also) be affected [2]. At present, there is no cure available for any form of genetic NMD that can completely stop (or reverse) the symptoms. Existing treatments including allied health care interventions such as occupational therapy, physical therapy and

speech therapy, focus on symptom relief and strategies to compensate for loss of functions. Because of the fundamental role that arm and hand movements play in everyday life, NMD may have a huge impact on the ability to perform daily activities and fulfil roles in life, which may influence the quality of life of the affected persons. Among types of NMD that have a significant impact on the ability to use the arm and hand in daily living are Facioscapulohumeral Dystrophy (FSHD), Limb-girdle Muscular Dystrophy (LGMD), Duchenne Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA) [3, 4]. Little is known about upper limb function in these diseases. The natural course of various types of NMD, including FSHD, LGMD, SMA, and DMD, has been described in the past [4]. This description was however mainly on the level of muscle function and structure in general. The level of activities, upper limb activities in particular, was hardly studied. More recently, the role of upper limb functions and their relation to activity limitations in children and adolescents with DMD has been investigated [5, 6]. Little is known, however, about impairments and their effects on upper limb activities and the participation in daily life in different types of NMD, including DMD, SMA, LGMD, and FSHD. Hence, these neuromuscular diseases are described below starting with DMD, which was the target group of the expert meeting described in chapter 2. The rest of this thesis mainly focuses on FSHD. In chapters 3 and 7, the two other neuromuscular diseases (SMA and LGMD) are addressed as well.

DMD

DMD is the most common form of muscular dystrophy in children. It is an X-linked recessive disorder, with an incidence of one in 6,000 male births [7]. Life expectancy in young men with DMD has increased from 14 years of age in the 1960s to about 30 years of age nowadays [8]. Although there is large variability in function [9], people with DMD generally have severely impaired motor functions. The ability to walk is impaired at first, but eventually also upper limb functions become severely impaired. Despite the limited distal motor functions, adult persons with DMD are often still able to perform certain daily hand activities. At later stages, when muscle strength diminishes further, people tend to lose this capacity [10]. In the teen years, upper limb impairments become more severe. The patterns of decline in upper limb functions of boys and men with DMD have been studied in detail by a member of our research group [5].

SMA

SMA is caused by degeneration of the spinal cord motor neurons, resulting in muscular atrophy and weakness. SMA is an autosomal recessive inherited type of NMD, and it is one of the most common NMDs in children with an incidence of about one in 12,000 live births [11]. SMA can be divided into four subtypes (type 1: severe, onset 0-6 months; type 2: intermediate, onset 7-18 months; type 3: mild, onset above 18 months; type 4: adult onset), based on the age of onset and the maximally achievable motor function. The clinical spectrum ranges from early infant death (type 1) to normal adult life with only mild weakness (type 4) [12]. Accept from SMA type 1, the disorder is slowly progressive. The upper limbs are usually stronger than the lower limbs [13]. Non-ambulant SMA patients tend to increase in upper limb strength until the age of 14 and tend to deteriorate afterwards [14]. It has been demonstrated that there is a gradual loss of muscle strength and physical functions in the upper limbs [15]. There is a broad range of functional capacities among people with SMA, from not being able to feed oneself to almost completely preservation of upper limb functions [16].

LGMD

LGMD comprises a group of autosomal dominant and autosomal recessive muscular dystrophies that primarily involve the pelvic and shoulder girdle muscles. There are many different types of LGMDs, with a variable clinical course, ranging from severe forms with rapid onset and progression to very mild forms. The prevalence of subtypes of LGMD in the population is also highly variable, depending on geographical and ethnic factors [17]. In LGMD, there is usually more weakness in the proximal muscles than in the distal muscles and in most people with LGMD, upper limb function is usually mildly impaired [18].

FSHD

FSHD is an autosomal-dominant, slowly progressive form of muscular dystrophy and the most common inherited muscular dystrophies in adults with an estimated prevalence in the general population of one in 8,000 [19]. FSHD causes mainly facial

weakness, clavicular flattening, scapula winging, and proximal muscle weakness in the upper limbs. In addition, many trunk and leg muscles may become involved, of which the abdominal muscles and foot elevators are affected relatively early in the course of the disease. Myopathic changes are seen in muscle biopsies, and recent studies showed muscle inflammatory pathology [20] and fat infiltration [21]. Because of the proximal muscle weakness, people experience difficulties while positioning their upper limbs in space. The severity of involvement is variable, ranging from facial weakness to generalized weakness, with eventually wheelchair confinement in about 20% of the people [22].

1.3 Upper limb interventions in NMD

Although no cure is available yet for any form of genetic NMD, life expectancy in for instance DMD has increased due to better healthcare and respiratory support. In combination with the many ICT solutions that have been developed in the last decade, people with NMD have potentially much better possibilities to participate in scholarly or work activities than ever before. Hence, interventions focusing on quality of life become more and more necessary. So far, current intervention programs have focused mainly on improving ambulation and less on improving or supporting arm function. While the possible harm of training interventions in NMD has been communicated for a long time, it has recently been shown that interventions like moderate-intensity resistance or aerobic training can be applied safely in NMD [23, 24]. In a recent study, it was demonstrated that the activity level, measured by the Motor Function Measure (MFM), did not decrease during a exercise training of six months in contrast to a control group receiving no specific training [6]. To improve the quality of life of people living with NMD who experience severe upper limb impairments, it is important to facilitate the performance of activities of daily living (ADL). One way to do that is to use assistive devices that augment arm function. In the past, various devices have been developed. These devices usually support the user by compensating part of the weight of the user's arm [25]. This type of device is called 'dynamic arm support' and can be subdivided into non-powered and powered devices [26]. Powered devices are meant for people with very limited to no muscle strength. Non-powered devices require a certain amount of residual muscle strength for accelerating and decelerating the upper limb to overcome friction and balancing errors [27]. Despite all developments

in designs, the number of users of dynamic arm supports is still low [28]. Various reasons have been mentioned for this situation: interfaces are too complex, supported range of motion is limited, device dimensions are too large, and support is insufficient due to clinical deterioration or the mere fact that a person prefers not to use supportive aids [28, 29]. Various initiatives aim to develop new devices that better suit the needs of the users. Examples of such developments are the McArm project (Box 1) and the Flextension A-Gear project (Box 2).

1.4 Upper limb measurement

To understand how exercise interventions or the prescription and use of devices could be improved, a good understanding of whether and how an intervention works is necessary. Systematic analysis of movements is required to investigate people's capacity to move the upper limbs. It is not only important to understand movement patterns from a biomechanical point of view, but also to relate this to activity limitations that people experience during daily life activities.

Movement capacity in controlled setting

Already in the 15th century, Leonardo da Vinci studied the structure of the human body, and he described the mechanical aspects during various movements [30]. Since then, many theories and experimental techniques have been developed to study the mechanical factors that play a role in the musculoskeletal system. These mechanical factors can be quantified using kinematic analysis [31]. Kinematics is the part of mechanics that describes the motion of points, objects, and systems of objects, without considering the masses of the objects or the forces acting on it [32]. The goal of any kinematic analysis is to develop a model that describes the motion of real-world objects. In human movement studies, kinematic examinations can be performed to model the functional performance of the limbs in normal and abnormal conditions [31]. The development of 3D motion tracking techniques (e.g. by using optoelectronic or accelerometric methods) has made digitally tracking of objects during movement accessible for widespread use. To analyze human movement kinematics, a lot of

Box 1: McArm project

The studies performed in this thesis were part of the McArm (Motion Controlled Arm support) project. This project was initiated by Focal Meditech BV, with the aim to develop a robotic arm support that can be controlled intuitively. Such arm support works on the basis of robot technology and is controlled by measuring minimal forces that the user still can generate in certain directions. Target users are mainly people with NMD or with stroke. The project had two main goals. The first one was to build two prototypes of a motion controlled 'dynamic arm support for use in daily life, and a training version to be used in virtual environments. A secondary goal was to investigate implementation of lightweight materials in the fabrication of new devices, such as carbon fiber. The development cycle began with the collection of usage and user requirements. In addition, previous developments and products have been closely reviewed. In a later stage of the project, it was attempted to convert the user requirements into technical specifications.

Figure 1: Prototype of motion control arm support

Box 2: Flextension A-Gear project

The objective of Flextension was to develop new support aids for the upper limbs that improve the quality of life for people with DMD. The initiative started in 2007 as a result of questions from the Duchenne Parent Project about what engineering and technology could do to improve the quality of life for boys with DMD. In 2009, an explorative study was performed to identify needs and requirements for a discrete, body-connected support aid that can be worn under the clothing and that can support an independent operation of the arm during primary daily activities (Figure 2) [29].

Since then, a group of researchers and developers have been working on the development of this device, in the A(bility)-Gear project. The focus of this project was to develop a passive arm support - controlled by the user, without motors - as well as an active arm support - powered by motors that are controlled by the user [33]. This project resulted in a new prototype that is a step towards inconspicuous and therefore well-received dynamic arm supports for people with muscular weakness (Figure 3).

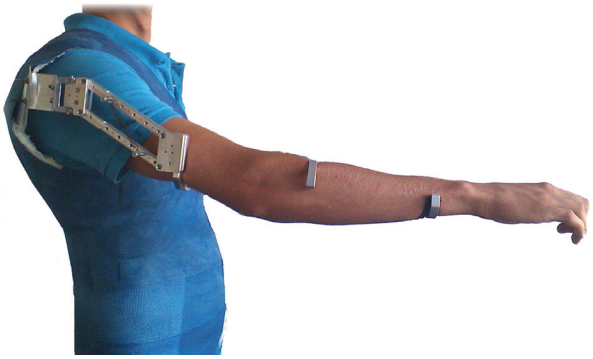

Figure 2: Concept of wearable arm support

Figure 3: New prototype of wearable arm support

kinematic variables are needed to describe all the movements of the different segments and joints of the body. To specify these variables, a kinematic model is required that simulates movement in the various types of anatomical joints and how these are connected by bony segments [31]. For the upper limb, a standard definition of such a model for the shoulder, elbow, wrist, and hand was proposed by Wu et al. in 2005 [34].

With the techniques that are available, the movement capacity of people with NMD can be investigated systematically under laboratory conditions.

To analyze neuromuscular control of movement in individuals with NMD, studying solely movement by kinematics is insufficient. It would also be helpful to know how different muscles are involved in performing the movements. Analysis of muscle involvement can be done by recording the electrical activity of the muscles that are formed by physiological variations in the state of muscle fibre membranes. These recordings are named electromyography (EMG). When EMG is used to record muscular patterns and coordination between muscles, it is called kinesiological EMG [35]. Clinical use of kinesiological EMG techniques has been focused primarily on lower extremity interventions, but potential applications for the upper extremities are indicated as well [36]. With kinesiological EMG, timing parameters such as the onset of muscle activity can be derived, as well as the magnitude of the EMG signal. The magnitude is regarded as an indicator of the contraction level of a muscle [36]. The combination of the use of kinematic and EMG analysis tools can, thus, help to assess the efficacy of training interventions and supportive devices.

Self-reported capacity in daily life

While investigating human movement and muscle involvement is useful to determine the physical function of a person, it provides only little insight into people's upper limb capacities and performance of daily life activities. Daily life activities involve a broad spectrum, from very basic activities such as reaching, grasping, and lifting, to more complex activities such as grooming, opening a door, preparing food, using a cell phone, etc. So far, basic upper limb activities have been assessed with, for example, the Brooke scale. This scale classifies activity limitations into six categories, varying from 'being able to lift both arms sideways in a full circle until they touch above the head, starting with the arms at the sides' to 'not being able to raise the hands to the mouth and not having useful function of the hands' [37]. However, there is little accurate information about limitations in activities that require more complex movements of the upper limbs. To investigate how capable people are to perform ADL, measures like the Capabilities of Upper Extremity (CUE) or the ABILHAND questionnaires may be more suitable. The CUE assesses basic upper limb capacities and the ABILHAND evaluates the ability to perform daily activities [38, 39]. The CUE contains 32 items

(30 items right/left arm, two items both arms) that can be scored on a 7-point scale (1 = unable to perform, 7 = can perform without difficulty). The ABILHAND questionnaire contains 22 items that can be scored on a 3-point scale (0 = impossible, 1 = difficult, 2 = easy). It is conceivable that upper limb activity limitations in patients with NMD will be related to lack of muscle strength, but limitations can also be influenced by pain and muscle or joint stiffness. The use of self-report measures like the CUE and ABILHAND can help to identify upper limb activity limitations that individuals with NMD experience in daily life. In combination with questions about pain and stiffness, for example, as used in the 'University of Michigan Upper Extremity Questionnaire' [40], activity limitations and participation restrictions related to pain and stiffness complaints can be identified.

1.5 Thesis outline

In the current thesis, the focus is on upper limb function in people with FSHD, one of the most common muscular diseases in adults characterized by significant problems in the positioning of the upper limbs in space. The conducted studies constitute part of a larger research line, in which upper limb function is also investigated in DMD and comparable NMD such as SMA and LGMD. In this thesis, upper limb function, activities, and participation of people with FSHD were compared to upper limb functioning in people with LGMD, SMA, and DMD. The aim is to find answers to the following research questions:

- What is known about upper limb function in patients with FSHD and how can upper limb function be measured?
- What activity limitations and participation restrictions do patients with FSHD experience in daily life, and are these comparable to those in DMD, LGMD and SMA?
- What is the influence of an arm support on upper limb use in patients with FSHD in daily life activities?

Because research on arm support in NMD is limited, an expert meeting was organized to discuss the necessities regarding arm function research in DMD and state-of-the-art requirements for assistive devices that can be used to support arm function. In this

workshop, the focus was on DMD because most research concerning arm function analysis and use of devices, so far, has been done in people with DMD. The outcomes are, however, also relevant for other types of NMD and are therefore described in **Chapter 2**.

Chapter 3 presents a literature review on arm function in people with FSHD and LGMD. In this chapter, the natural course upper limb function and measures to study such function in these two groups is presented.

Chapter 4 investigates which upper limb activity limitations people with FSHD experience in daily life. These limitations are investigated using self-reported outcome measures at the level of body functions (pain and stiffness), daily life activities and societal participation.

Chapter 5 describes the results of a study in which arm movements and the involvement of specific muscles are investigated with kinematic and EMG tools in a group of people with FSHD and in healthy people during the performance of motor tasks in a movement laboratory.

While the use of arm supportive devices has been investigated before, in for example healthy elderly and people who have had a stroke, the changes induced by arm supports in person with FSHD are unknown. In **Chapter 6**, the effect of an arm support on arm kinematics and EMG activity is explored in individuals with FSHD as well as in healthy individuals.

To investigate whether comparable profiles of upper limb function can be identified in various types of NMD (i.e. FSHD, LGMD, DMD, and SMA), the same self-reported questionnaires are used. **Chapter 7** describes the reported upper limb impairments and activity limitations in people with FSHD compared to those with LGMD, DMD, and SMA.

Chapter 8 contains a summary and general discussion, including clinical implications, based on the studies reported in this thesis. In addition, future perspectives will be contemplated.

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2

1st Workshop on Upper-Extremity Assistive Technology for Duchenne: state of the art, emerging avenues, and challenges

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2.1 Introduction

Workshop theme and participants

The 1st workshop on Assistive Technology for people with Duchenne Muscular Dystrophy (DMD) was held in London (United Kingdom), on April 27th 2015. The primary goal was to bring people from different disciplines together and discuss opportunities to accelerate the development of upper-extremity assistive technology for enhancing the functional abilities of non-ambulant men with DMD. The topics of the workshop included the state of the art, emerging avenues and challenges of upper-extremity assistive technology. Twenty-four participants representing parents, experts in user requirements, human-machine research, electrical and mechanical engineering, and clinicians involved in the care of children with Duchenne muscular dystrophy from Denmark, the Netherlands, the UK and the USA, participated in the workshop. Key results included the identification of the need for comparative studies based on standard requirements and outcome measures, and the low acceptance rate of commercially available devices. Advanced robotic arm supports are still in experimental phase. Finally, focus groups were initiated on (1) evidence based user requirements and acceptance, (2) assessment protocols, (3) modular technology, and (4) accessibility and reimbursement.

DMD and assistive technology

DMD is a progressive muscle disorder, characterized by muscle wasting and weakness. The first signs of the disease is ambulatory delay, with 50% of DMD boys starting to walk after 18 months [1]. DMD leads to full time use of a wheelchair in the mid-teens, loss of upper-extremity (UE) function in the late-teens followed by the development of cardiomyopathies and respiratory failure [1, 2]. Currently, there is no cure for DMD, and treatment is mainly aimed at delaying disease progression and preserving functional abilities. Due to these new treatments (including nocturnal ventilation), life expectancy

in boys with DMD has increased from 14 years of age in the 1960s to 25 years of age in the 1990s [3, 4]. Currently, the median survival of boys with DMD is estimated to be over 30 years [5, 6] and it is expected that the life expectancy will continue to increase. Because of the prolonged life expectancy, the number of individuals living with DMD is increasing. This group of young men live with impaired UE function for more than 15 years, which severely limits the performance of basic activities of daily living (like self-feeding and personal care) and restrict social participation. It is generally accepted in the DMD community that early and combined efforts of steroids and bracing to preserve leg strength are rewarded by a longer ambulatory period. There is also evidence that suggests that certain assisted arm training delays the progression of muscle weakness in the arms [7]. The use of assistive devices has the potential to improve the quality of life for people with DMD, by enabling them to continue performing activities of daily living and participate in social activities. Between 1936 and 2011 [8], more than 100 UE assistive devices have been developed. Most of them are intended for rehabilitation to regain strength and motor control, and few are designed to assist during activities of daily living. UE assistive devices for daily use are also known as dynamic arm supports. Despite all the developmental efforts, few devices are commercially available. Van der Heide et al. [9] concluded that only a few number of dynamic arm supports that have been developed have also been evaluated. Most of the studies that they found examined the effects of dynamic arm supports on body functions, activities, and participation under laboratory conditions. Although, in general, these studies report positive outcomes, the number of users of dynamic arm supports appears to be low. Researchers have mentioned various possible reasons that could be the cause of the low number of users: preference of compensatory movements over using an assistive device, large dimensions of the devices that stigmatize the user, difficulties in adjusting the device, clinical deterioration and expense. Besides efficacy evaluation under laboratory conditions, a much better understanding of effectiveness of using dynamic arm supports in daily life is needed [9].

2.2 User requirements

Patients perspective

Elizabeth Vroom presented what the highest priorities are for young men with DMD. In order to improve quality of life for those living with Duchenne, independence and participation must be facilitated. For young men, it is important to be able to participate in work and social activities. While privacy is indicated as being important, socialization and employment are priorities as well. In 2007, the Dutch Duchenne Parent Project organized a workshop to determine whether improving arm or leg function should be prioritized. The outcomes of this workshop were that young men considered arm function as the highest priority. The loss of lower extremity function, can be compensated fairly well by using a wheelchair, but compensating the loss of arm function is less evident [10]. Although complete loss of arm function arises at the late-teens, it has been shown that performing activities with the arms is already limited in the late ambulatory stage and that participating in school activities is also restricted because of these limitations [10]. When young men with Duchenne were asked what a new drug should gain in terms of daily activities, the responses were related to the activities that can be achieved with the arms: touch face, self-feed, personal care such as brushing teeth, toileting, use of computer, ability to maneuver wheelchair are considered of high value. Individuals with DMD expressed an urgent need for privacy, which becomes impossible as weakness increases. Two user requirements studies have been performed to determine what activities are considered to be most important. Annie Kennedy presented the results from a study performed by the PPMD in the USA. The results from focus groups sessions were combined with an online survey that was distributed in the USA (N=19), to determine priorities of ambulant and non-ambulant people with DMD. The priority activities for the ambulant group were stand up, pick up objects from the floor and walk upstairs. The priority activities for the non-ambulant group were repositioning at night, bring hands to mouth, shift while seated, using joystick and using the keyboard of a computer.

Imelda de Groot presented the results from a World-wide survey. In this survey, 213 individuals (age ranging from 1.5 to 35.2 years old) with DMD participated, of which 95 were ambulant and 118 non-ambulant. From this survey, there was concluded that the

main priority is to eat independently and prepare food. Subsequently, activities that were indicated to be important by the ambulant respondents were get dressed, reach to objects or lift objects and writing. Activities that were indicated being important by the non-ambulant respondents were personal hygiene, drinking and using a computer [10].

Discussion and Future Actions

- Arm function is highly important. More insight in ADLs that should be supported and what people require from an arm support is needed. Current surveys address what young men value (e.g., use of computer). It is important to reach out more broadly in getting input into device design—it might just be that we are currently sampling a small portion of the population who is willing to test a novel device. It is also important to consider potential users in the full range of the progression, from early through late loss of ambulation.

- Studies on technical requirements are needed (e.g. required movement speed, number of degrees of freedom, range of motion of each joint). While there is a considerable variety of upper-extremity assistive devices, there are few studies that investigate the user requirements. One example is the study by Ramanathan et al. [11], which analyzes the arm trajectories of healthy subjects during ADL to find what are the movements that an arm support device should assist.

- The use of two arms may be preferred over one arm, since a lot of ADL are bimanual tasks. Current devices are essentially for one arm, therefore bimanual application doubles the price. Insurance companies typically reimburse at most one arm support.

- Patient organizations have a crucial role in putting patients first, encourage collaborations, recognize unmet needs, determine which initiative has the highest priority, leverage research funding, stimulate regulatory approval, improve the access of technology and advocacy in the reimbursement of devices.

2.3 Evaluation of Arm function

In order to optimize devices and assess effectiveness of devices, quantitative and objective evaluation methods are needed. Quantitative data comprises kinematic parameters, such as the range of motion of supported arm movements and the muscle effort that is needed to using a particular type of arm support. Individuals with DMD need relatively more effort in all directions in order to perform the same movements as healthy controls. Also, they recruit more muscles simultaneously for all motions. One key question is whether muscle activation requirements or the amount of energy is required to perform a specific activity will become lower by using the assistive device.

Disease Progression and Training Effects

In the same World-wide survey (N=213) that was presented by Imelda de Groot, changing patterns of arm function during the course of DMD were investigated. The questionnaire included the domains of pain and stiffness in the arms, activity limitations and restrictions in social participation. In general, pain, stiffness, and activity limitations increased with disease stage. The researchers found that activity limitations in the arms already occurred in the early ambulatory stage, and that these limitations affected their social participation. About 70% of the respondents experienced limitations when performing social activities. Only 9% of the respondents on the other hand used supportive aids [10]. Progressive muscle weakness results in reduction of physical activity and disuse of the musculoskeletal and cardiorespiratory systems, because performing activities cost more and more energy [12]. In addition, the use of a motorized wheelchair and a sedentary lifestyle further restricts the arm function, resulting in secondary physical deterioration and disuse. To decrease the deterioration due to disuse, arm training is considered [13]. There is evidence that assisted bicycle-like motion training of the legs and arms is feasible and safe for both ambulant and wheelchair-dependent children [7]. Recently, a training study in DMD was conducted, in which participants received a training program with a dynamic arm support. The training was based on a virtual reality computer game, in which participants had to perform several ADL while using dynamic arm support. Six boys finished the study and in four of these six boys, the trained arm retained more motor function than the

untrained arm. These preliminary findings may indicate that boys with DMD can safely train their arms with dynamic arm support [14].

Range of Motion

Jay Han presented part of his work on measuring reaching workspace. In order to quantify the reachable workspace, various methods can be used. One promising method is the Kinect-acquired reachable workspace measure, developed at the University of California. This method comprises a scalable and affordable sensor-based upper extremity reachable workspace assessment system using a Kinect sensor [15, 16]. This quantitative reachable workspace outcome measure has demonstrated applicability as a novel surrogate marker of upper extremity function in DMD and Becker Muscular Dystrophy (BMD) [17]. In a series of preliminary studies, the reachable workspace outcome measure has shown its validity, reliability, and sensitivity, as well as clinical-meaningfulness by correlating strongly with person-reported activities of daily living (ADL) function. Additionally, the Kinect-acquired reachable workspace measure demonstrated its utility in both ambulatory and non-ambulatory individuals as well as pediatric and adult populations with DMD/BMD, providing for the first time, a means to follow progression of the disease through important clinically-meaningful functional milestones, such as both the loss of ambulation and ability to self-feed, through the lifespan of an individual with DMD or BMD. The impact of the novel upper extremity assessment tool and outcome measure will be most directly felt in clinical trials where it will facilitate: 1) access to clinical studies for non-ambulatory individuals, 2) reduction of study participant burden, 3) improvement in efficiency through automation, 4) home-based data collection via internet-connected sensor, and 5) better evaluation of efficacy for interventions; all contributing to potentially transform the way clinical trials are conducted in DMD/BMD. However, improved quantitative measurements of upper extremity with its correlative clinical data will also have implications for intervention development in the robotics field. The kinematic and dynamic parameters obtained across a large cohort with a spectrum of disease severity and functional levels can be used to inform design of assistive devices, robots, and exoskeletons. The data will also be informative in general model building as well as refining models of upper extremity function. Identification of individual requirements/needs and functional parameters will contribute to a more ‘personalized’ and prescriptive robotic system that will be optimized and tailored to individual functional needs.

Discussion and Future Actions

- Arm function progression studies: Monitoring the disease progression is needed so that engineers know what level of assistance is needed as a function of time (per day, per year) in arm supports. To this end modeling may be useful to estimate individual muscle function.

- How much support is needed: A current problem is that the arms are often disused, which results in deterioration of muscle capacity. Once people with DMD lose ambulation, the arm use is reduced. The general consensus was to keep using the arms, but also that overuse should be avoided. There is a need to address upper extremity function, with titrating how much assistance is given. Although it is not scientifically clear when there is overuse, fatigue, pain and no functional return the next day are associated with upper extremity overuse and can be used to help titrate the amount of assistance required.

- There is a need for outcome measures to evaluate arm function in a daily life setting: Currently insufficient objective data is available to evaluate how much the arms are used/burdened during the day. Also longitudinal studies are missing.

- Therapeutic effects: Pilot studies suggest that there may be a therapeutic effect when a person regularly uses an arm support. How does this therapeutic effect relate with the quality of life of the users? Is it necessary to prevent overuse of the arms?

2.4 State of the art and current research

Commercial Arm Supports

The first arm supports were developed in the 1960's [8]. While the first designs only supported eating movements, current devices assist a wide range of ADL. Up to date, there is a large number of UE assistive devices that have been developed, but only few are intended for daily use, commercially available and used by people

with DMD. Extensive reviews can be found in [8] and [18]. Dynamic arm supports can be divided into two subcategories, non-powered (also called passive, or body-powered devices) and powered devices (also known as active or externally-powered devices). Non-powered arm supports use elastic elements (i.e. springs) to compensate the weight of the arm. Tariq Rahman, Paul Verstegen and Blake Mathie presented the developments of the WREX, the arm supports of Focal Meditech and the X-Ar respectively. The WREX (JAECO Orthopedic, USA) [19] and the TOP (Focal Meditech BV, the Netherlands [20]) arm supports are non-powered arm supports that have been in the market for more than 20 years. The WREX (JAECO Orthopedics, USA) is now available in two versions: the metal version that attaches to the wheelchair or to a table, and a wearable version that combines 3D printed plastic parts and metal parts, known as Baby WREX, for ambulatory children [21]. More recent commercially-available non-powered arm supports include the SLING, the Dowing and the Balancer (Focal Meditech BV, the Netherlands [20]), the VERTICAL M.A.G (Proteor, France), the Nitzbon Mobility Arm (Nitzbon, Germany), the Saebo MAS (Saebo Inc., USA) and the X-Ar (Talem Technologies, USA [22]). Powered arm supports use motors to change the settings of the gravity compensation mechanism or to move the arm in the vertical or horizontal plane using a joystick or buttons. The TOP arm support can be extended with an actuator, called HELP, to provide active support in the vertical direction to assist persons with more severe muscle weakness. Beside the TOP/HELP, Focal Meditech has developed the active version of the Sling, Darwing and the GoWing. Other powered arm supports include the Armon (Microgravity Products, NL) [23], the Zonco Mobile Arm Valet (ZoncoArm, USA) [24], the DAS (Exact Dynamics, the Netherlands) [25] and the Neater Arm support (Neater Solutions, UK) [26]. A recent systematic review on the effect, effectiveness and usability of arm supports concluded from the results of 47 evaluation studies that there was an increased ability to perform activities of daily living and user satisfaction when using an arm support, but that the use of dynamic arm supports at home was low [9]. A recent study of a questionnaire-based evaluation of the WREX concluded that the WREX made a significant improvement in arm function for users while performing everyday tasks. Sixty percent of the 55 users included in the study continued to use the WREX at the time of the survey. Sixty-nine percent of wheelchair-mounted WREX users continue to use it, and 48% of body-mounted continue to use it. Reasons for abandonment included weight, interference with other activities, joint contractures, and imprecise gravity compensation. Users showed more improvement of arm function with the wheelchair-mounted WREX than the body-mounted model. Aesthetics, fitting, and reimbursement were identified as

areas for improvement [27]. Furthermore, a user evaluation study with the Neater arm support concluded that the use of the Neater arm support by adults and teenagers with neuromuscular disorders could greatly improve their independence, confidence, and ability to engage in social situations [28].

Current Research on Arm Supports

In addition to currently available devices there are several initiatives that aim to develop solutions that better suit the needs of young men with DMD. Among these initiatives are: the A-Gear project (DPP-Flextension, The Netherlands), the ReachABLE project (New Jersey Institute of Technology, USA) and the Patient@Home project (Aalborg University, Denmark). Micha Paalman and Joan Lobo-Prat presented the work done in the Flextension A-Gear project. The Flextension A-Gear project started in 2011 with the goal of developing an inconspicuous arm support that could adapt to the growing needs of people with DMD. The development towards the ultimate arm support was divided in two separate functional prototypes: the Passive A-Gear and the Active A-Gear, which are directly related to two levels of assistance. The Passive A-Gear is intended for younger individuals that are still able to perform activities of daily living when the weight of the arms is compensated. The Passive A-Gear, in contrast to the existing arm supports, has a mechanical structure that closely follows the biomechanics of the arm and trunk, uses a novel spring configuration to balance the weight of the arm, and has a hip joint incorporated to allow flexion/extension movements of the trunk [29]. When the support provided by the Passive A-Gear becomes insufficient, the Active A-Gear will provide the extra assistance in weaker individuals with DMD using motorized joints. In order to operate active arm supports the user needs to communicate his motion intention to the device through a control interface. The selection of the control interface in response to specific user needs and capabilities is a crucial determinant of the usability of the arm support. In previous studies, we have shown that the use of electrical activity of arm muscles (known as surface electromyography, sEMG) or the measurement of small forces that are still generated by the muscles, are both suitable signals to derive the motion intention of the adults with DMD with very limited arm function and control active arm supports [30]. When using force-based control it is crucial to accurately distinguish the voluntary forces from the intrinsic forces of the arm such as gravity, inertia or stiffness forces. Especially for persons with a severe muscle weakness the intrinsic forces of the arm have to

be compensated. An alternative method is EMG-based control. Although the use of muscle activity is less intuitive, the EMG signals are not affected by the intrinsic properties of the arm such as stiffness, and therefore directly represent the motion intention of the user. On the other hand, disadvantages of EMG-based control include the poor long-term signal. In [30] we found that while movements with the force-based control were smoother and faster, EMG based-control was perceived as less fatiguing. Madeline Corrigan gave an overview of the ReachABLE project, which is carried out by the New Jersey Institute of Technology (NJIT). This project aims at developing a wheelchair mountable admittance controlled arm support to increase independence for activities of daily living for individuals with DMD. A proof-of-concept prototype has been developed to demonstrate the feasibility of implementing force-based control with motorized antigravity assistance to provided intuitive, compliant, and inherently safe user control [31]. Force-based admittance control allows the minimization of the friction and inertia that opposes the user's movements, which decreases the overall force required to control the device. Admittance control allows the intuitive use of residual muscle strength to operate the device. The use of residual muscle strength has the potential to reduce disuse atrophy and the development of contractures. Because admittance control involves modelling the device as a small point mass, the device can be tailored to the functional status of each individual. The mass can be decreased as the strength of the user decreases over time to continue to allow control of the device despite the change in muscle capacity. Conversely, the mass can be marginally increased, as needed, to promote use of the muscle strength that remains in order to promote use of residual strength that can potentially reduce disuse atrophy [31]. Musculoskeletal models have been widely used to investigate the upper-extremity biomechanics. Musculoskeletal models can be implemented to objectively analyze the interaction between the user and the arm support. The manufacturing of an upper-extremity assistive device is an expensive process and patient-specific musculoskeletal models hold a large potential for design optimization of such devices. By co-simulating musculoskeletal model and orthosis dynamics, the properties of the orthosis can be adjusted to obtain an optimal design to augment the residual capabilities of a specific patient. However, to achieve this, a patient-specific model that takes into account the properties of the musculoskeletal system, including the pathology, must be developed and validated. Miguel Nobre Castro presented part of his work in which he modeled the upper-extremity of a patient with idealized brachial plexus injuries (BPI), from which paralyzed/atrophied muscles were known. This model contains 10 joints and 134 muscle-tendon units and by using inverse dynamic analysis internal forces (muscles

and joint reactions) were estimated [32]. The co-simulation of the patient model with a passive orthosis model was performed taking advantage of patient's residual muscles function during a 'pick a cup and drink' task. This study suggested that a BPI patient with an idealized C7 nerve root lesion could be assisted by an orthosis whose set of springs' stiffness was optimized. Design optimization promotes experimentation and design maturation before the manufacturing stage as long as the subject and orthosis models are accurate. Clinical validation of these prototypes is mandatory to assess the function of the orthosis under operating conditions.

Discussion and Future Actions

- The adoption rate of commercially available arm supports is low: There are several potential reasons that limit the user's acceptance of arm supports: current devices have large dimensions, which compromises their attractiveness and they do not provide enough support for the weaker users. It is important to determine the variables behind the adoption or rejection of arm supports and how to weigh those variables in the design and deployment process. There is a need of studies that investigate which user requirements are not met. There is also a need to incentivize the use of arm supports to preserve arm function.

- There is a need for evaluation of current arm supports. There are several arm supports on the market and it is not clear what are the capabilities and limitations of each of them. A quantitative and objective evaluation of the performance of each arm support and their working principles could result in a set of guidelines for choosing which arm support is the most suitable for a specific user.

- It is not clear whether users prefer wearable devices or devices that require wheelchair attachment: Both wearable and wheelchair based devices present advantages and limitations. Most of the commercially available devices are wheelchair bound and new developments are focusing on wearable arm supports.

- A clear image of certification and reimbursement in various countries is needed: To get devices reimbursed, cost-benefit studies are needed. Although it is difficult, quality of life and costs need to be justified. Such cost-benefit studies

are needed from both the individual using the device and their caregiver. One of the challenges is to progress from anecdotal feedback to reliable statistics.

2.5 Emerging Avenues

Soft Robotics

Conor Walsh presented his vision on the next generation wearable robots, in which he foresees use of soft materials such as textiles and elastomers to provide a more conformal, unobtrusive and compliant means to interface to the human body [33–36]. These robots will augment the capabilities of healthy individuals (e.g. improved walking efficiency, increased grip strength) in addition to assisting patients who suffer from physical or neurological disorders. Various projects focus on the design, fabrication and control principles that are required to realize these systems. An example is a soft exosuit that can apply assistive joint torques to restore mobility of those with physical disability [33, 34]. Advantages of this suit over traditional exoskeletons are that the wearer's joints are unconstrained by external rigid structures, and that the worn part of the suit is light, which minimizes the suit's unintentional interference with the body's natural biomechanics. There has been demonstrated that healthy subjects required 7% less muscle activation when the used the exosuit. A second example is the development of a soft robotic glove for hand rehabilitation that consists of a wearable textile with attached elastomeric fluid-powered actuators specially designed to match the natural movements of the fingers and thumb [35, 36]. A similar glove is also being tested at usability in persons with muscular dystrophies. Part of the technology is open source available via a Soft Robotics Toolkit.

Shell-based mechanisms

Just Herder shared his vision on the possibilities of compliant shell-based mechanisms (or shell mechanisms for short), a class of mechanism between conventional linkage based exo-robotic systems and soft robotics, in body support devices. Shell mechanisms is the extension of the idea of statically balanced compliant mechanisms [37–39]

into the third dimension in the form of spatially curved shells that are to be designed for specified stiffness. This technology bears the promise of true exoskeletons that could be wearable underneath regular clothing. This means that the functionality of exo-robotic systems, which tend to be bulky and stigmatizing, needs to be fitted into a design space of around 10 mm around the body contour. Statically balanced shell mechanisms are excellent candidates for achieving this challenging goal. Herder his team is currently working in this direction by developing dimensional optimization methods based on isogeometric analysis, and semi-automated graphical synthesis methods. The initial results are promising although there are still challenges to be overcome. Future developments include extension of shell-mechanisms to distributed mechatronic systems where motion, actuation and sensing are distributed over the surface of the shells.

Control modalities

Aldo Faisal gave an overview of the possibilities of eyetracking as control modality for assistive devices. He explained that the pursuit of an effective brain machine interface holds the hope to enable patients with severe motor disorders to interact with their surroundings. Different approaches can be categorized as non-invasive cortical interfaces (e.g. EEG), invasive cortical interfaces, e.g. implanted multi-electrode arrays (MEA), or non-invasive and non-cortical interfaces (e.g. EMG). The clinical aim, however, remains the same: to extract an intention signal from a patient, for which conventional approaches such as joystick, mouse movement or sip and puff control are not possible. Present 'assistive technology' interfaces can serve most of its possible users. Operating however is still as slow as 10-15 years ago (e.g. abundant use of scan systems that almost always solve the problem, but inhibit speedy task performance), not intuitive or too complex. The use of a combination of intention signals for example eye movements and muscle activity has the potential to realize fast and easy to learn control interfaces with a very little latency. Based on the idea 'Seeing is moving', Faisal and his collaborators applied an eye-tracking based control interface into the control of a wheelchair. In the European project ENHANCE, similar approaches are used to develop control interfaces for active arm and hand support devices.

Trunk, head and hand support

Bart Koopman and Arno Stienen presented some of the latest developments in trunk, head and hand support devices. Persons with DMD often have instability of the trunk and head leading to balance problems while sitting. Scoliosis is often present and negatively affects trunk posture. Control of trunk posture is not only essential for respiration and to avoid swallowing problems, but also for optimal function of the arm and for positioning of the head to make visual control of the arms possible. Arm support enables persons with DMD to continue use of the arms and hand by being able to position the hand in a larger area around the body. However, bringing the arm further away from the body destabilizes trunk posture, which limits use of the arm support. Given these problems, stabilization of the trunk is often necessary. However, this currently involves restriction of the degrees of freedom of the trunk and hence arm/hand function. In addition, current trunk stabilizing braces and supportive devices are often uncomfortable, cause pain and induce respiratory problems, feeding problems, and potentially pressure sores. New solutions are required that stabilize trunk and head postures while allowing the user to choose postures that support optimal performance of hand/arm activities. It is crucial that the assistance provided by devices is adapted to actual needs of those with Duchenne. Too much help may have the price of adding to muscle loss, so has to be titrated carefully. Beside the importance of adaptive trunk and head support, adaptive support of hand function may be essential for persons with DMD in late non-ambulatory. In order to realize such adaptive supports, control of the device and minimal dimensions are important factors. A good understanding of the progression of the weakness in different muscle groups is needed to build better devices. Biomechanical models may also be useful. It is however difficult to develop a kinematic model, so it is important to collect lots of date which is made available for the community.

Discussion and Future Actions

- Are the expectations from robotic solutions realistic?: While emerging technologies are very attractive from a technical point of view, it is important to keep in mind that there is a need for functional, robust and affordable assistive devices. The high rate at which these emerging technologies are advancing is a clear

indication that there is global interest in developing better assistive devices that can improve the quality of life of people with DMD.

- Share best practices, and things that did not work: A mailing list involving the workshop participants and others interested, that is updated (with a résumé) regularly, including new publications and products.

2.6 Conclusion

At the end of the workshop, John Porter and Just Herder gave a summary of the workshop's contents and chaired the discussion between the workshop's participants. The workshop addressed the user requirements, the current methods for the evaluation of arm function, the commercially available arm supports, the current research projects towards active arm supports, and emerging technologies that could be useful for the future development of assistive technology for people with DMD. Based on these discussions, six clusters of action points were identified. These are (a) identifying user and caregiver needs and acceptance, (b) assess performance of user and caregiver before and after fitting of a device, (c) develop lab and ambulant testing metrics and protocols, (d) gather data on use of device, (e) develop modular technology and (f) work on accessibility and reimbursement in different countries. These action points were distributed over four focus groups, namely on (1) evidence based user requirements and acceptance, (2) assessment protocols, (3) modular technology, and (4) accessibility and reimbursement. The ambition of these groups is to accelerate progress in these focus areas by coordinating cross-border research and development efforts and identify opportunities for governmental and industrial funding.

2.7 Workshop Participants

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Annie Kennedy, Parent Project Muscular Dystrophy, USA
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3

Upper extremity function and activity in facioscapulohumeral dystrophy and limb-girdle muscular dystrophies: A systematic review

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Abstract

Objective: The aims of this review were 1) to provide insight into the natural course of upper-extremity (UE) impairments and UE activity limitations associated with facioscapulohumeral dystrophy (FSHD) and limb-girdle muscular dystrophies (LGMD), and 2) to provide an overview of outcome measures used to evaluate UE function and activity in patients with FSHD and LGMD.

Methods: Scientific literature databases (PubMed, MEDLINE, EMBASE, CINAHL and Cochrane) were searched for relevant publications. Inclusion criteria: 1) studies that included persons with a diagnosis of FSHD or LGMD; and 2) studies that reported the natural course of the UE functions and/or activity with outcome measures at these levels.

Results: 247 publications were screened, of which 16 fulfilled the selection criteria. Most studies used manual muscle testing (MMT) to evaluate UE function and the Brooke Scale to evaluate UE mobility activities. The clinical picture of UE impairments and limitations of UE activities in FSHD and LGMD patients was highly variable. In general, FSHD and LGMD patients experience difficulty elevating their upper extremities and the execution of tasks takes considerably longer time.

Conclusions: The clinical course of UE impairments and activity limitations associated with FSHD and LGMD is difficult to predict due to its high variability. Although measures like MMT and the Brooke Scale are often used, there is a lack of more specific outcome measures to assess UE function and UE capacity and performance in daily life. Measures such as 3D motion analysis and EMG recordings are recommended to provide additional insight in UE function. Questionnaires like the Abilhand are recommended to assess UE capacity and accelerometry to assess UE performance in daily life.

3.1 Introduction

Muscular dystrophies encompass a group of more than 30 inherited myopathies that are characterized by progressive muscle wasting and weakness. Patients with certain forms of muscular dystrophy become symptomatic in infancy or childhood, whereas others may not become symptomatic until middle age or later. Although the various muscular dystrophies vary in their severity and progression, all types are generally progressive, disabling over time. Upper-extremity (UE) function is often impaired due to muscle weakness [1], which may result in limitations in daily activities and fatigability [2]. However, little is known about the severity, course, and impact of UE impairments and limitations. Facioscapulohumeral dystrophy (FSHD) and limb-girdle muscular dystrophies (LGMD) are two types of muscular dystrophies in which loss of UE function is prominently present. Both FSHD and LGMD are slowly progressive and have a typical age of onset between 10 and 30 years of age[1]. FSHD is an autosomal-dominant, slowly progressive form of muscular dystrophy and one of the most common inherited muscular dystrophies with an estimated prevalence in the general population of 1 : 21,000[3, 4]. It is characterized by initial signs of weakness in the muscles of the face and shoulder girdle, but the pattern and severity of subsequent muscle affliction in FSHD are highly variable[5, 6]. LGMD comprises another group of autosomal muscular dystrophies that primarily involve the pelvic and/or shoulder girdle muscles. LGMD includes several sub-types with distinct rates of progression of muscle weakness and patterns of activity limitations. The prevalence of sub-types of LGMD in the population is highly variable, depending on geographical and ethnic factors[7].

Currently, there is no cure for muscular dystrophies. However, treatment and management can consist of medication, surgery and/or rehabilitation services including strength training, training of aerobic capacity or the use of aids and adaptations such as arm supports to enable the performance of daily activities[8–10]. For the development of effective training programs for the UE, and innovative motion controlled arm supports, a better understanding of the natural course of UE function and activity in FSHD and LGMD is needed.

The aims of this systematic review were 1) to evaluate the natural course of UE impairments and UE activity limitations associated with FSHD and LGMD and 2) to provide an overview of the outcome measures used to evaluate the natural course of UE function and activity in FSHD and LGMD patients.

3.2 Method

Search strategy

A search of the PubMed, MEDLINE (1948 – 2013, week 40), EMBASE (1980 – 2013, week 40), CINAHL and Cochrane databases was performed using the MeSH terms and free text words “fshd” OR “facioscapulohumeral” OR “limb girdle muscular dystrophy” in combination with “upper extremity” OR “arm” OR “hand”. Potentially relevant publications were also identified by manually searching through the citations listed in the retrieved articles.

Selection criteria

Articles that contained an abstract and were written in English, Dutch, German or French were included. Studies were selected when they 1) included participants with a clinically or genetically confirmed diagnosis of FSHD or LGMD and 2) reported the natural course of UE functions and/or activities with outcome measures at these levels. Studies were excluded in case the full-text article was not available or if UE function was described as part of an intervention such as surgery, that would influence the natural course following FSHD and LGMD, or might introduce a selection bias in the research population due to the aim of the intervention.

Procedure

The first author (AB) assessed the titles and abstracts and saved the references that appeared to be relevant. In the case of doubt, the abstract was assessed by a second

reviewer (EC) and the results were discussed until consensus was reached. The two reviewers then decided whether to include or exclude each article based on the detailed information contained in the full-text article. The first author also scanned the reference lists of the included articles to identify additional articles for potential inclusion. Additional articles that fulfilled the selection criteria were retrieved for a more detailed evaluation. Final inclusion or exclusion of each article was based on an independent assessment by two reviewers (AB and EC).

Each study was evaluated on three domains of the International Classification of Functioning, Disability and Health (ICF) relevant to assess the use of the UE in daily life [11]. These domains were UE functions (ICF b7), UE mobility activities (ICF d440/d445) and self-care activities and domestic life activities (ICF d5/d6). For each article, the study's aim, design, inclusion and exclusion criteria, and the characteristics of the participants (including age, gender and duration of symptoms) were recorded (if reported) in addition to the outcome measures, results and conclusions (Tables 1 and 2).

3.3 Results

Selection of studies

Our search of the online databases yielded 247 articles (see Figure 1). After assessing the titles and abstracts, 215 of these studies were excluded because the type of participants and/or the outcome measures did not meet our predefined criteria. The full-text articles of the remaining 32 studies were retrieved and assessed for eligibility. Of these 32 articles, one could not be accessed, and 19 did not meet the selection criteria. A manual citation tracking search yielded an additional four articles. Thus, the final selection included a total of 16 articles.

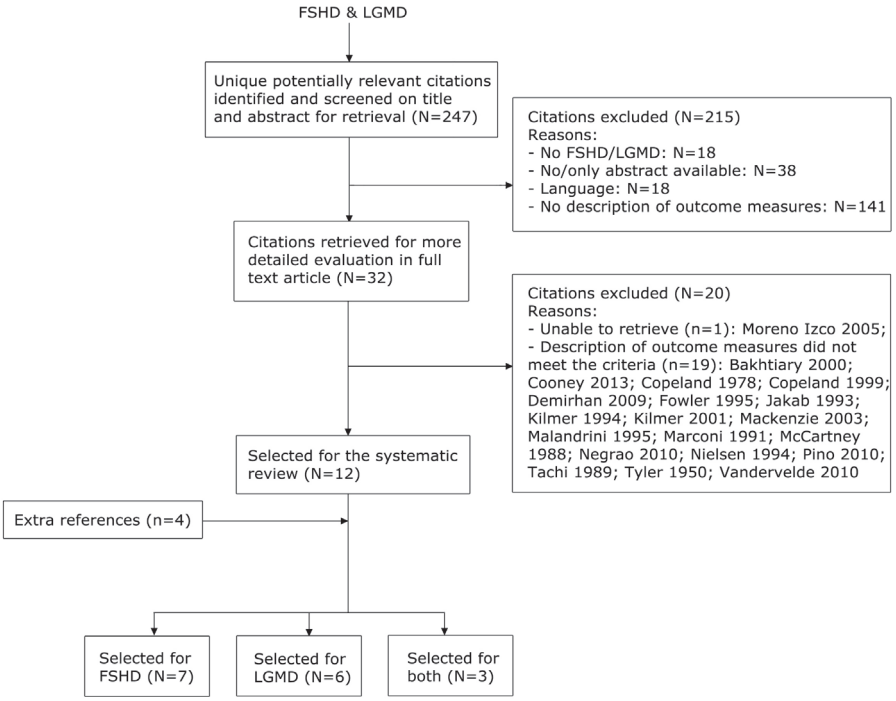

Figure 1: Flowchart showing the search and the inclusion and exclusion of articles

Table 1: Studies of arm function in patients with FSHD

Author (year)	Aims	Design	Inclusion /exclusion	Subjects	Outcome measures arm functions and activities	Results/Conclusions
Brouwer et al. (1992)[12]	Investigate asymmetry of muscle weakness of the shoulders and arms in FSHD patients and determine whether this asymmetry is related to handedness	Comparative study including patients with FSHD and healthy controls	*FSHD:* I: Well-defined autosomal dominant FSHD. E: children under 15 yrs of age. *Healthy subjects:* E: no neurological abnormalities or recent muscle weakness or pain in arms or shoulders	53 patients, 35M, 18F; mean age 44,6yrs; 24 healthy controls, 16 M, 8 F; mean age 36yrs; Duration of symptoms: FSHD: M: 23 yrs (range 0-54yrs); F: 19 yrs (range 0-49).6 M and 2 F with FSHD were asymptomatic.Onset of first symptoms between 15 and 30 yrs 0-9: 26%10-19: 26%20-29: 28,6%>29: 19,5%;Age at onset 0- 9: 19,5%10-19: 39%20-29: 14,3%>29: 27,3%	*UE functions* Muscle strength during performance of MVC with hand held dynamometer in: flexors, extensors, abductors, external and internal rotators of the shoulder; extensors and flexors of the elbow; extensors of wrist; flexors of fingers and thumb. *UE mobility activities* No outcome measures *Self-care activities and domestic life activities* No outcome measures	*UE functions* Asymmetry in muscle involvement; unknown which muscles are active when testing muscle groups; Abductors (up to 90°), flexors and extensors of the shoulders are affected most. Insufficient scapular fixation could play a role. External rotators more affected than internal rotators, which might explain the internal rotation of the arms in FSHD patients. Forearm muscles were spared. Wrist extensors and elbow extensors relatively strong in F, which might be related to the shorter duration of symptoms in F.R-handed FSHD patients are stronger in the muscles of the L side, which is in contrast to the healthy controls.
FSH-DY Group (1997)[13]	Develop valid, measures for documenting the clinical course of FSHD; examine issues of clinical and genetic heterogeneity; provide the basis for effective design of future therapeutic trials in FSHD.	Prospective cohort study with follow up every 6 months up to 36 months	I: diagnostic and eligibility criteria reported by Tawil et al.[14] E: Cases suggestive of x-linked or recessive mode of inheritance	81 patients, 35M, 46F; mean age 39.0±13.4yrs; duration of symptoms	*UE functions* Manual muscle testing (MMT), Maximum Voluntary Isometric Contraction (MVIC) during elbow flexion/extension, and shoulder abduction, external rotation, horizontal adduction/abduction. *UE mobility activities* No outcome measures *Self-care activities and domestic life activities* No outcome measures	*UE functions* Variation in age at onset and duration of symptoms; 20% 'normal' arm function; All muscles involved in most patients; Medians of MVIC ranged from 2.3 to 5.0 sd below average normal; proximal arm muscles often prominently involved; some patients little or no force; Scores homogeneous in shoulder muscles in contrast to other muscles; No sign. difference in degree of involvement in males/females, the latter more heterogeneous; no significant relationship between age and strength; slight tendency for older patients to be less affected; Young age at onset (<20yrs) and long duration of symptoms (>20 yrs) tended to have poor muscle strength on average; generally small differences between sides and large asymmetry in some patients not related to dominance; Decline over time noted with both MVC and MMT in elbow flexion/extension, but not evident in the shoulder region; Slow but significant progression over time not associated with age, gender, age at onset or duration of symptoms.

Kilmer et al. (1995)[15]	Develop an impairment and disability profile for FSHD	Prospective cohort study with 10 years follow up	I: FSHD diagnosis based on criteria of Munsat(15) E: individuals with scapula-peroneal syndrome.	53 patients, 32M, 21F; Mean age 38±13yrs; Age at onset 16+9 yrs; Duration of symptoms 21±13yrs	*UE functions* MMT (n=22), isometric strength, and isokinetic strength measures passive ROM (n=22) *UE mobility activities* Timed Motor Performance (TMP) (n=22), Brooke (n=22) *Self-care activities and domestic life activities* No outcome measures	*UE functions* Extensor muscles weaker than flexors, proximal muscles weaker than distal muscles ;Asymmetry of the arm muscle groups with more weakness of selected dominant limb muscles; Shoulder external rotators, shoulder abductors and wrist extensors sign. weaker in the dominant limb; An early age of onset (<15) associated with greater likelihood of more severe weakness; Significant slow decline of overall MMT of 0.22 units per decade of age; Isometric and isokinetic strength of all muscle groups sign. less in FSHD; for isometric strength a disease-gender interaction was found: male FSHD patients more weakness compared to controls than female patients; Overall isometric strength was reduced in FSHD patients of 46% for elbow flexors, 58% for elbow extensors, 47% for shoulder flexors and 63% for shoulder extensors; Grip strength in FSHD was significantly weaker than in the control group in dominant, but not in non-dominant limb. This side-to-side difference was not the case for pinch strength; Isokinetic elbow strength was reduced about 46%, no significant side-to-side differences were found in the elbow flexion strength *UE mobility activities* Brooke scores: Brooke 1: 32% (n=7); Brooke 2: 23% (n=5); Brooke 3: 41% (n=9); Brooke 4: 5% (n=1); It took 2-6 times longer for FSHD patients to perform TMP tasks; No correlation between Brooke score or TMP tests and age or disease duration.
Lord et al. (1987)[16]	Determine UE/LE relation based on Vignos and Brooke scale	Cohort study of various NMD	I: age >6y with diagnosis FSHD	10 patients with FSHD (total of 90 patients in study), 6M, 4F; Mean age 46.6yrs; Mean age at onset 18,4yrs; Mean disease duration 28,2yrs	*UE functions* MMT on 36 muscle groups *UE mobility activities* Brooke Scale *Self-care activities and domestic life activities* No outcome measures	*UE functions* MMT results not described in article *UE mobility activities* FSHD: Brooke 1: 20% (n=2); Brooke 2: 30% (n=3); Brooke 3: 30% (n=3); Brooke 4: 20% (n=2); Brooke 5: 0% (n=0); Brooke 6: 0% (n=0).
Lue et al. (2000)[17] (2009)[18]	Asses muscle strength, motor functions and independence in ADL in FSHD population in Taiwan [18]. Assess accepta-bility of the scales to evaluate the functional status of patients with various types of MD [18]	Cohort study	I: A definite diagnosis of FSHD confirmed by 2 neurologists based on clinical and genetic analyses, and EMG and muscle biopsy criteria, according to the diagnostic criteria for neuromuscular diseases from the European Neuromuscular Research Group used at that time E: any other coexisting medical or psychiatric disease	20 patients, 12M, 8F; Mean age 35.5±16.6yrs, range 13-80 yrs; Average age of onset 18,2+7,4 yrs, range 9-30yrs; Average disease duration 17.3±14.5yrs, range 4-70yrs mean age 35.8±8yrs; range 23-50yrs	*UE functions* MMT of shoulder flexors, extensors,abductors; elbow flexors,extensors; wrist flexors,extensors;Grades: normal strength (5), good grade (4), fair grade (3), poor grade (2), trace grade (1) and zero grade (0). Minus (-) and plus (+) symbols mean + and – 0,33. *UE mobility activities* Brooke scale *Self-care activities and domestic life activities* Barthel Index (BI) (range 0-100); Scores: 0-20 totally dependent, 21-61 severely dependent, 62-90 moderately dependent, 91-99 mildly dependent	*UE functions* MMT overall (mean of 32 muscle groups): 3.8±0.6 (range 2,7 – 4,7); Mean strength shoulder 2.8; mean strength elbow 3.6; wrist least impaired (strength 4.3); Presence of a progressive asymmetrical muscular weakness; Average arm muscle strength significantly weaker than leg muscle strength; Shoulder muscle groups weaker than other muscle groups; Mean muscle strength of right arm significantly weaker than left; mean muscle strength not correlated to age of disease duration; Extensors not weaker than flexors. *UE mobility activities* Brooke scores: mean 2.3 + 0.8 (1-3); Brooke 1: 20%(n=4), Brooke 2: 30% (n=6), Brooke 3: 50% (n=10); Brooke 4-6: 0%; Floor effect in 20%, no ceiling effect;Brooke scale not correlated to age of disease duration; Brooke scale too simple to identify functional changes in patients with slowly progressive MD. *Self-care activities and domestic life activities* Average value of Barthel was 97,8 + 4,7 (range 85-100); 80% (n=16) was totally independent, 20% (n=4) was moderately independent; BI was not correlated to age or disease duration but was significantly correlated to mean muscle strength; The appropriateness of the BI for evaluating ADL in FSHD is questionable.

Personius[33], Tawil et al.[14]	Present protocol design and reliability studies of various measures of strength and functional ability and preliminary baseline results to document clinical course of FSHD	Comparative cohort study with patients with FSHD and healthy controls	I: FSHD evidence of facial weakness, scapular fixation, or foot dorsiflexor weakness E: other myopathies that mimic clinical of FSHD, neuropathic disorder	32 patients, 16M, 16F; mean age 36.1±9.6 yrs; range 17–49 yrs; 32 age/gender matched controls: mean age 35.8±8 yrs; range 23–50 yrs	*UE functions* Manual muscle testing MMT with MRC scale) and Quantitative muscle testing (QMT) (MVIC with QMT machine) of the following muscle groups: shoulder abductors, external rotators, horizontal abductors, horizontal adductors, elbow flexors and elbow extensors; Grip (Jamar dynamometer and pinch Jamar pinch gauge) measurements *UE mobility activities* No outcome measures *Self-care activities and domestic life activities* No outcome measures	*UE functions* In FSHD group, the strength of the shoulder abductors was less than half the strength of the shoulder abductors in the healthy controls; In the FSHD group, the strength in shoulder abductors of both arms was nearly the same; in horizontal abduction, the right arm was stronger than the left arm; In most muscle groups the muscles of the right arm were stronger than the muscles of the left arm; The strength in the FSHD group was 43% (shoulder abductors) to 60% (elbow extensors) of the strength of the healthy controls; Average standardized QMT score ranged from 1.7–3.6SD below average normal performance, across the muscle groups; Despite small side-to-side differences, the large asymmetry in some patients not related to dominance.
Rozman et al. (2001)[19]	Develop methodology for torque measurements of the elbow flexors	Cohort study of various NMD	Not described	7 patients with FSHD (total of 49 patients in study), 5M, 2F; mean age 36yrs	*UE functions* Isometric measurement of the torque elicited by maximum voluntary elbow flexion (MVEF), using a specially designed electronic brace. Three MVEF lasting about 3 s separated by a pause of 3 s. About 15 s later the last MVEF was produced, for 30 s. The half-fatigue times defined as the times spent within the period from maximum torque to its one-half value were calculated. *UE mobility activities* No outcome measures *Self-care activities and domestic life activities* No outcome measures	*UE functions* Patients with FSHD had longest half-fatigue time and elicited the lowest mean torque in both the short MVEF (0.29 Nm) as well as in 30 s-long MVEF.
Stübgen et al. (2010)[20]	Chart the rate of clinical disease progression by 6-monthly assessments of strength and function by study a relatively homogeneous subgroup of patients with FSHD with measurable weakness and functional impairment	Prospective study with 10yrs follow up	E: Not diagnosed according to criteria of FSHD consortium(19)I: relatively advancedstage of disease (inability to raise straightened arms above horizontal level)	16 patients, 12M, 4F; mean age 58.8yrs (at end study); duration of symptoms, 38.4yrs (at end study)	*UE functions* MMT (MRC scale) in the following muscle groups on both sides: shoulder abducors, external rotators, horizontal abductors, and horizontal adductors, elbow flexors and extensors; A composite measure of strength was calculated *UE mobility activities* Brooke scale *Self-care activities and domestic life activities* Modified items on BI: reach out to objects on bed table, wash and brush hair, applying make-up, pulling vest or sweater overhead, put on brassiere, writing, winding a watch, folding a handkerchief and holding a newspaper	*UE functions* 50% showed functional deterioration of the arms during the 10yrs study period. *UE mobility activities* Brooke at end study: Brooke 1: 0% (n=0), Brooke 2: 0% (n=0), Brooke 3: 13% (n=2), Brooke 4: 75% (n=12), Brooke 5: 13% (n=2), Brooke 6: 0% (n=0) *Self-care activities and domestic life activities* An inverse correlation between total ADL score and AMS ($p<0.001$ at onset; $p = 0.002$ at 10 years). Patients needed assistance with activities such as reaching for objects on the bed table (weak shoulder muscles) or sitting up in bed (weak abdominal muscles). Activities like standing up from/sitting down on an easy chair, the center of a couch or the floor became more difficult mainly due to weakened shoulder girdle and abdominal muscles.

Table 2: Studies of arm function in patients with LGMD

Author (year)	Aims	Design	Inclusion /exclusion	Subjects	Outcome measures arm functions and activities	Results/Conclusions
Lord et al (1987)(16)	Determine UE/LE relation based on Vignos and Brooke scale	Cohort study of various NMD	I: age >6y with diagnosis LGMD	24 patients with LGMD (total of 90 patients in study), 13M, 11F; Mean age 47 yrs; disease duration 21.7 yrs	*UE functions* MMT on 36 muscle groups *UE mobility activities* Brooke scale *Self-care activities and domestic life activities* No outcome measures	*UE functions* MMT results not described in article *UE mobility activities* Results of 24 LGMD patients are mixed with results of 5 patients with Becker muscular dystrophy; Brooke 1: 55% (n=16), Brooke 2: 17% (n=5), Brooke 3: 17% (n=5), Brooke 4: 4% (n=1), Brooke 5: 7% (n=2), Brooke 6: 0% (n=0)
Lue et al (2000)[21]	Reach better understanding of muscle strength, motor function and activity of daily living in patients with LGMD	Cohort study	E: any other coexisting medical or psychiatric disease	48 patients, 29M, 19F; Mean age 39.4±15.2yrs, range 12-76yrs; Average age of onset 21.7±13.7yrs, range 3-51yrs; Average disease duration 17.5±12.6yrs, range 3-64yrs	*UE functions* MMT *UE mobility activities* Brooke scale *Self-care activities and domestic life activities* BI range 0-100; Total scores are broken down into severity categories: 0–20 totally dependent, 21–61 severely dependent, 62–90 moderately dependent, 91–99 mildly dependent, and 100 totally independent	*UE functions* Progressive symmetrical limb girdle muscular weakness; mean muscle strength inversely related to disease duration. No sign. difference between strength of extensor and flexor muscles nor between dominant and non-dominant sides *UE mobility activities* Mean Brooke score 2.3±1.3 (range 1-5); Brooke 1: 33,3% (n=16); Brooke 2: 20,8% (n=10); Brooke 3: 35,4% (n=17); Brooke 4: 0%; Brooke 5 10,4% (n=5) and Brooke 6: 0% *Self-care activities and domestic life activities* Average BI 85.3±20.8 (range 5-100); 47,9% (n=23) totally independent; 8,3% (n=4) mildly dependent; 29,2% (n=14) moderately dependent; 12,5% (n=6) severely dependent and 2,1% (n=1) totally dependent.Mean muscle strength sign. correlated with BI and Brooke scales; BI and Brooke score sign. correlated.
Lue et al (2009)[18]	Assess acceptability of the scales for evaluating the functional status of patients with various types of MD	Cohort study	I: A definite diagnosis of LGMD E: Excluded if patient had any other coexisting medical or psychiatric disease	54 patients with LGMD (total of 154 patients in study), 32M, 22F; Mean age 39.3±15.6yrs, range 12–76yrs; disease duration 17.4 ± 12.2yrs, range 2–64yrs	*UE functions* no outcome measures *UE mobility activities* Brooke scale *Self-care activities and domestic life activities* Barthel Index range 0-100; Total scores broken down into severity categories: 0–20 representstotally dependent, 21–61 severely dependent, 62–90 moderately dependent, 91–99 mildly dependent, and 100 totally independent	*UE mobility activities* Mean Brooke scale: 2.3±1.3 (1-5); Brooke 1: 37% (n=20), Brooke 2: 18,5% (n=10), Brooke 3: 33,3% (n=18), Brooke 4: 0% , Brooke 5: 11,1% (n=6), Brooke 6: 0%; Floor effect present in 37% of persons with LGMD and no ceiling effects *Self-care activities and domestic life activities* Average BI 85.6±20.2 (range 5-100). 1 subject (1.9%) totally dependent; 7 (13%) severely dependent; 17 (31.5%) moderately dependent; 3 (5.6%) mildly dependent and 26 (48.1%) totally independent.None of the subjects showed a floor effect and in 48% of the subjects was a ceiling effect.

Mahjneh et al (2001)[22]	Describe a 23-year follow-up of a family where 10 members are homozygous for the same frameshifting dysferlin mutation	Prospective study, with 23 years of follow up	I: homozygous dysferlin mutation (LGMD2B)	10 patients, 8M, 2F; age range 17-76yrs; duration of symptoms 3-33yrs (three patients died during the follow-up of 23yr)	*UE functions* Physical examination, MMT *UE mobility activities* six stage scale 1) Flexes arm when carrying 5 kg Can abduct arm at 90° when carrying 5 kg, and at 180° when carrying a 2 kg; 2) Flexes arm when carrying 2 kg. Can abduct arm at 90° when carrying 3 kg, and at 180° when carrying 2 kg; 3) Flexes arm when carrying 1 kg. Can abduct arm at 90° when carrying 2 kg, and at 180° when carrying 1 kg; 4) Flexes arm when carrying 1 kg. Can abduct arm at 90° when carrying 1 kg and at 180° when carrying 0.5 kg; 5) Flexes arm, unable to carry weight. Can abduct arm at 90° and at 180°, unable to carry weight; 6) Flexes arm without weight to 150°. Cannot abduct arm >45° *Self-care activities and domestic life activities* no outcome measures	*UE functions/UE mobility activities* The weakness in the upper limbs remains mild and is confined to the proximal muscles in most patients (stages 3-4); upper arm muscle involvement about 7 years after lower limb girdle; weakness most pronounced in biceps, less so in triceps, pectoralis, rhomboid, infraspinatus and supraspinatus. Deltoid and trapezius affected very late. Latissimus dorsi and small hand muscles relatively spared; Winging of scapula not present in early stages, but in late stages deficient adduction observed of lower edge of scapulae in six patients
McDonald et al (1995)[23]	Develop an impairment and disability profile for three types of LGMD	Prospective cohort study with 10 years follow up	I: LGMD diagnosis based on criteria of Walton[24] E: individuals with scapulohumeral and quadriceps myopathy types or dystrophin abnormalities	66 patients, divided in three groups: ARMDC (19), ADLO (18) and PF (29); ARMDC: mean age 42±4yrs, age at onset 9±4 yrs, disease duration 33±3yrs; ADLO: mean age 50±11yrs, age at onset 33±6 yrs, duration of symptoms 23±16yrs; PF: mean age 43±17yrs, age at onset 22±12 yrs, duration of symptoms 25±14yrs;	*UE functions* MMT (shoulder, elbow wrist and thumb), isometric strength, and isometric (shoulder and elbow, pinch and grip) and isokinetic (elbow) peak torque ROM (elbow and wrist) (n=46) *UE mobility activities* Brooke (n=22); Timed Motor Performance (TMP): cut 3x3 square *Self-care activities and domestic life activities* No outcome measures	*UE function* All types of LGMD: Proximal muscles weaker than distal muscles; No difference between dominant and non-dominant side; No age or disease duration effects on ROM found. ARMDC is the most rapidly progressive type of LGD for both proximal and distal muscle groups. ARMDC: No difference between flexor and extensor muscles in shoulder, elbow and wrist; MMT scores declined per decade disease duration. Reduction of >20° in 23% of the subjects in range of motion at the elbow, 17% in wrist. ADLO: Elbow flexors stronger than extensors; no difference between flexors and extensors in shoulder and wrist; Significant declines in MMT scores per decade disease duration; Reduction of >20° in 20% of the subjects in the wrist and none in the elbow. PF: Elbow flexors weaker than extensors; no difference between flexors and extensors in shoulder and wrist; decline per decade disease duration in trunk and extensors; reduction of >20° in 5% of subjects in elbow, 5% in wrist. *UE mobility activities* All types of LGMD: TMP tests more slowly in several patients. ARMDC: Brooke scale: 15% grade 1-2, 54% grade 3, 31% grade 4-6;84% relied on wheelchair (62% full-time). ADLO: Brooke scale 60% grade 1-2, 20% grade 3, 20% grade 4-6; 39% relied on wheelchair. PF: Brooke scale: 70% grade 1-2, 20% grade 3, 10% grade 4-6; 31% relied on wheelchair (5% full-time).

Rozman et al (2001)[19])	Develop methodology for torque measurements of the elbow flexors	Cohort study of various NMD	Not described	11 patients with LGMD (total of 49 patients in study), 5M, 6F; Mean age 34.6yrs	*UE functions* Isometric measurement of torque elicited by MVEF, using a specially designed electronic brace; Three MVEF that lasted about 3 s and separated by a pause of about 3 s. About 15 s the last MVEF for a period of 30 s.The half-fatigue times (times spent within the period from maximum torque to its one-half value) also calculated for each group. *UE mobility activities* No outcome measures *Self-care activities and domestic life activities* No outcome measures	*UE functions* Patients with LGMD had similar mean half-fatigue time and elicited similar torque of both short and 30s long elbow flexions.
Stübgen et al. (1994)[25]	Investigate correlation functional disability with degree of weakness and disease duration and rate of disease progression	Cross-sectional and retro-spective	I: inheritance pattern, phenotype described in detail, EMG consistent with active, chronic myopathy, muscle histopathology showed dystrophic lesions	20 patients, 13M, 7F; mean age 40.5yrs, range 22-67; mean age of onset 21.1yrs,range 12-60; mean disease duration 18.9yrs,range 6-42yrs	*UE functions* Average muscle score (AMS); MMT of movements around neck, shoulders, elbow and wrists with MRC scale converted to a 0-10 point system. *UE mobility activities* Brooke scale and interval analysis of Brooke scale by asking patients to recall from memory how long after disease onset they had reached the various functional “milestones” if applicable *Self-care activities and domestic life activities* BI	*UE functions* Poor correlation between global weakness and patient age; inverse relation between global strength and duration of disease ($r=-0.48$; $p=<0.05$); wheelchair bound patients sign weaker than ambulant group ($p<0.002$), mean AMS resp. 3.5 and 6.9. *UE mobility activities* No patient lost useful hand function; Even in fourth decade of illness, some patients maintained useful hand function above shoulder level; Brooke scores: Brooke 1: 39% (n=7), Brooke 2: 0% (n=0), Brooke 3: 28% (n=5), Brooke 4: 22% (n=4), Brooke 5: 11% (n=2), Brooke 6: 0% (n=0); Brooke scores with mean disease duration: Brooke 1:38% (n=20), 12.6±6.6yrs (range 2-22), Brooke 2: 23% (n=12), 13.3±7.8yrs (range3-26), Brooke 3: 23% (n=12), 15.5±8.5yrs (range 4-26), Brooke 4: 13% (n=7), 16.4±8.3yrs (range 8-28), Brooke 5: 4% (n=2), 28.0±1.4yrs (range 27-29), Brooke 6: 0% (n=0); wide ranges in disease duration at which disability milestones were reached. *Self-care activities and domestic life activities* Average value of BI was 61±32 (range 31-120). Inverse relation between AMS and total ADL score ($r=-0.82$, $p=<0.0001$); relation between disease duration and total ADL score ($r=0.76$, $p<0.0001$)
Stübgen et al (1997)[26]	Prospectively monitor progression of weakness, functional impairments. and ADL abilities in relation to age and disease duration	Prospective follow up study with follow up of 6 years	I: inheritance pattern, phenotype described in detail, EMG consistent with active, chronic myopathy, muscle histopathology showed dystrophic lesions	19 patients, 12M, 7F; Mean age 47.2±12.5yrs, range 28-73yrs; Mean disease duration 25.2±9.7yrs, range 12-48	*UE functions* AMS; MMT of movements around neck, shoulders, elbow and wrists with MRC scale converted to a 0-10 point system. *UE mobility activities* Brooke scale *Self-care activities and domestic life activities* BI	*UE functions* No significant deterioration in muscle strength; Variation in change of muscle strength not related to the degree of weakness, disease duration, or age; no significant change in strength in the 6 strongest or 6 weakest patients. *UE mobility activities* Brooke 1: 26% (n=5), Brooke 2: 16% (n=3), Brooke 3: 5% (n=1), Brooke 4: 21% (n=4), Brooke 5: 26% (n=5), Brooke 6: 5% (n=1); 70% of patients lost at least one grade in the arms and/or legs; 10 patients (53%) lost a functional grade of the arms; No correlation with age, disease duration or degree of global muscle weakness. *Self-care activities and domestic life activities* No significant change on BI index; significant functional deterioration in 30% of patients with predominant involvement in a single functional domain; variation between patients; deterioration of the ADL score correlated with the loss of functional grades.

Stübgen (2008)[27]	Monitor clinical disease progression in 2nd interval (10y) by re-assessment of MMT, Brooke and BI	Prospective follow up study with 10yrsinterval	I: inheritance pattern, phenotype described in detail, EMG consistent with active, chronic myopathy, muscle histopathology showed dystrophic lesions	18 patients, 11M, 7F; mean 55.4yrs, range 38-81yrs; Mean disease duration 33.9 yrs,range 22-47yrs	*UE functions* Average muscle score (AMS); MMT of movements around neck, shoulders, elbow and wrists with MRC scale converted to a 0-10 point system. *UE mobility activities* Brooke scale *Self-care activities and domestic life activities* BI	*UE functions* Significant decline of limb strength independent of age or disease duration and more rapid in stronger patients. *UE mobility activities* Brooke scale; 8 patients (44%) lost at least one functional grade over the past decade and 14 patients (78%) lost at least one functional grade during 17yrs(1989-2006); The 7 most functional patients (grade 1) all lost at least one functional grade, only one patient lost two grades. Four patients reached a functional grade 5 during the study period. Two patients entered the study at grade 5 but did not deteriorate further to reach the worst grade. *Self-care activities and domestic life activities* The mean ADL score for 18 patients was 58.3 (in 1989), 65.6 (in 1996), and 77.2 (in 2006). The total ADL score deteriorated significantly between 1989 and 1996 (P =0.045) and significantly during the periods 1996 to 2006 (P = 0.001) and 1989 to 2006 (P <0.001); correlation between the ADL score and disease duration (P = 0.043) and a sign. negative correlation between ADL and AMS (P <0.001)

ADL = Activities of Daily Living; AMS = Average Muscle Score; BI = Barthel Index; EMG = Electromyography; E = Exclusion criteria; F = female; I=Inclusion criteria; LE = Lower Extremities; M = male; MD = Muscular Dystrophy; MMT = Manual Muscle Testing; MRC = medical research council; MVC = Maximum Voluntary Contraction; MVEF = maximum voluntary elbow flexion; MVIC = Maximum Voluntary Isometric Contraction; NMD = Neuromuscular Disease; ROM = Range of Motion; TMP = Timed Motor Performance; UE = Upper Extremities; Yrs = years

FSHD

Studies and patients included In our search, 10 articles were identified that described UE functions and/or activities in patients with FSHD, based on the description of eight study cohorts (Table 1). These studies comprised a total of 272 patients (153 males and 119 females). The mean ages of the patients in the studies were 36 to 59 years (with a range from 13 to 80 years). The mean duration of symptoms was 17 to 38 years (with a range from 0 to 54 years), and the mean age at onset was 16 to 18 years (with a range from 9 to 30 years).

Outcome measures Each study used outcome measures at the level of UE function. Four of these studies also included measures at the level of UE mobility activities [16, 20, 28, 29], and two studies included outcome measures at all three levels[17, 20]. One study by Stübgen [20] also included follow-up measurements at all levels (Tables 1). To evaluate UE function, six of the studies performed manual muscle testing (MMT) of 18-36 muscles [13, 14, 16, 18, 20, 28], a clinical evaluation method to grade the strength of muscle groups [30]. Several studies assessed maximal isometric and isokinetic muscle strength by measuring maximum voluntary contractions (MVC) force [12–14, 19] and two studies measured grip strength and pinch strength by handheld dynamometry [12, 14]. One study measured the passive range of motion in the joints [28] and one study recorded half-fatigue time (defined as the time interval between maximum torque and half-maximum torque)[19]. With respect to outcome measures at the level of activity, five of the studies used the Brooke scale[14, 16, 17, 20, 28], which is a scale that ranges from 1 to 6 and is used to classify basic UE mobility activities (a higher score indicating more severe limitation)[31]. One of the studies measured the time required to complete a certain task[28]. One study used the Barthel Index (BI)[32], a general Activities of Daily Living (ADL) score that ranges from 0 to 100 (with a higher score indicating better ADL)[17], and one study used a modified BI in which a higher score indicates poorer ADL performance[20].

UE function According to Brouwer et al.[12], the muscles that are most severely affected in patients with FSHD are the muscles that abduct the shoulder above 90º (deltoid), the shoulder anteflexors (deltoid, pectoralis major and subscapularis) and the shoulder extensors (deltoid and latissimus dorsi). The authors also indicated that the extensor muscles are weaker than the flexors, that the external rotators are

more severely affected than the internal rotators, and that the forearm muscles are largely spared. Brouwer et al. [12] found that the wrist extensors and elbow extensors are relatively strong in women compared to men. Kilmer et al.[28] concluded that, compared to healthy controls, male patients show more severe muscle weakness than female patients. On the other hand, the FSH-DY Group[13] reported no significant difference in the degree of muscle involvement between men and women. Several studies reported asymmetric muscle strength; some studies indicated that the dominant arm (or the mostly used arm) is the weaker arm[12, 17, 28]. Tawil et al.[14] found that the right side of the body was usually weaker than the left side, but they found no correlation with handedness. No consensus was reached among the various studies with respect to the relationship between age and strength. For example, the FSH-DY Group[13] found no significant correlation between age and strength; the slow but significant progression of the disease over time was not associated with age, gender, age at onset or the duration of symptoms. In contrast, Kilmer et al.[28] found a slow but steady progressive decline in strength per decade of age, with the proximal muscles being weaker than the distal muscles and the extensor muscles being weaker than the flexors. Similarly, the FSH-DY Group[13] and Kilmer et al.[28] found that an early age of onset (under the age of 15 years) was associated with more severe weakness, and the FSH-DY Group additionally concluded that patients with a relatively long duration of symptoms (>20 years) tended to be more severely affected.

UE mobility activities In five of the studies, the Brooke scale was used to evaluate basic UE activities [14, 16, 17, 20, 28]. Combining the scores from four studies [16, 17, 20, 28] comprising a total of 68 participants, approximately 60% of the patients scored either a 3 (unable to raise the hands above the head but able to raise a 250-ml glass of water to the mouth) or a 4 (able to raise each hand separately to the mouth, but unable to raise a 250-ml glass of water to the mouth). Only two of the participants scored a 5, while none scored a 6. Kilmer et al. [28] also measured Timed Motor Performance (TMP) and found that FSHD patients took 2 to 6 times longer to perform a TMP task than healthy controls, but found no correlation of Brooke scores or TMP tests with age or disease duration.

Self-care activities and domestic life activities Lue et al. [17] found an average BI score of 97.8 + 4.7 (range: 85-100) in their patients. In their cohort, 80% (n=16) of the patients had a maximum score of 100, meaning that they were completely independent. In the same research group, they found a significant correlation between BI and mean

muscle strength, but no correlation between BI and age or disease duration [17, 18]. Also Stübgen et al. [20] found a correlation of BI with mean muscle strength and not with age or disease duration.

LGMD

Studies and patients included Nine articles describing UE impairments and/or activity limitations in patients with LGMD were identified by our search strategy (Table 3). Each article described a prospective or cross/sectional cohort study, with a total of 270 patients, including 123 men and 81 women (one study including 66 patients did not report gender [23]). The mean age of the included patients was 35 to 55 years (with a range of 12-81 years), and the mean disease duration was 17 to 34 years. The age of onset also varied widely and was dependent on the type of LGMD [23].

Outcome measures Eight of the studies reported outcome measures at the level of UE function[16, 19, 21–23, 25–27], eight studies measured UE mobility activities [16, 18, 21–23, 25–27], and five studies included measures of self-care and domestic life [18, 21, 25–27]. Four of the studies collected follow-up measurements [22, 23, 26, 27]. To evaluate UE function, seven studies manually tested 18-36 muscles [16, 21–23, 25–27], and two studies assessed maximal isometric and isokinetic muscle strength by measuring MVC [19, 23]. One study measured grip strength and pinch strength [23], and another study performed physical examinations to evaluate posture and stability of the scapula [22]. Another study recorded half-fatigue time, which is defined as the time spent between maximum torque and half-maximum torque [19]. With respect to measuring outcome at the level of activities, seven studies used the Brooke scale [16, 18, 21, 23, 25–27] [16, 18, 23, 25, 27-29], and one study used a self-created six-points scale to measure basic activity [22]. One study measured the time required to complete a given task [23]. Three studies used the original BI [25–27], and two studies used a modified BI in which the scores were distributed among severity categories [18, 21].

UE function Lue et al. [21] reported that LGMD is characterized by a progressive symmetrical weakness of the limb girdle musculature. Mahjneh et al. [22] reported that this weakness often remains mild in the UE, that proximal muscles are weaker than distal muscles, and that UE muscle involvement typically lags behind the involvement

of the lower limb girdle by several years (with a delay of approximately seven years). McDonald et al. [23] found a progressive decline in muscle strength per decade of disease duration. Stübgen et al. [26] found no changes in strength over a period of six years, but found a significant decline in UE muscle strength after ten years [27]. Because of these findings, Stübgen [27] concluded that the change in muscle strength was independent of both patient age and the duration of the disease, but that the change in muscle strength seemed to progress more rapidly in stronger patients. No differences were found between the dominant and non-dominant sides [13, 16].

UE mobility activities Pooling the scores from five studies [16, 18, 21, 23, 25] with a combined total of 225 patients revealed that 55% of the participants scored Brooke scale 1-2, 30% scored a 3, and 15% scored 4-6. An exception is the patient group with rapidly progressive autosomal recessive muscular dystrophy of childhood (ARMDC), 54% of whom scored Brooke scale 3 and 31% scored Brooke scale 4-6 [23]. Stübgen et al. [26] found that 53% of the 19 patients in their follow-up study deteriorated by at least one grade over six years, and this deterioration was not correlated with age, disease duration or the degree of muscle weakness. In the next follow-up study, Stübgen et al. [27] reported that eight out of 18 participants with LGMD lost at least one functional grade over a decade, although none of the participants reached the worst grade. Mahjneh et al. [22] used a different scale to evaluate basic skills based on six stages (with a higher stage indicating poorer performance). Most of their patients scored a 3 or 4, meaning that they could flex their arms when carrying a 1-kg weight and abduct their arms to 90° when lifting a 2- or 1-kg weight (representing stages 3 or 4, respectively), and that they could abduct their arms to 180° when carrying a 1- or 0.5-kg weight, respectively. McDonald et al. [23] found that several of their patients performed the TMP tests more slowly.

Self-care activities and domestic life activities In both studies by Lue, only one patient was in the category of being totally dependent, approximately 30% of the patients were moderately dependent, and 48% were completely independent [18, 21]. In the follow-up studies conducted by Stübgen [26, 27], the activities of daily living (ADL) scores did not change significantly.

3.4 Discussion

The aims of this systematic review were to get insight in the natural course of UE impairments and activity limitations in FSHD and LGMD, and to provide an overview of the used outcome measures.

In the current review, UE outcome measures were evaluated at two levels of the ICF: the level of UE functions and UE activities namely mobility, and self-care and domestic life activities. For the UE activities, capacity and performance can be evaluated. Capacity describes an individual's ability to execute a task or an action and performance describes what an individual does in his or her current environment and [11].

To evaluate UE function in FSHD and LGMD patients, MMT is the most commonly used method. Some authors argue that MMT is a rather subjective method for assessing isometric muscle strength [19], whereas others claim that it is a valid and sensitive measure of disease progression in patients with Duchenne muscular dystrophy [33]. In current review, it was not possible to compare MMT results between various studies, as most of the studies reported a composite score of strength instead of reporting scores for the various UE muscle groups. The studies examined in this review used a variety of methods, making comparisons difficult and precluding the pooling of data from multiple studies. Bakhtiary et al. [34], who investigated the effect of motor learning, studied UE muscle activity and movement patterns by using electromyography (EMG) rather than MMT. These researchers found that EMG activity during a simulated drinking task was higher in the FSHD group than in healthy controls. The muscle activity and movement patterns in the FSHD group included more synergistic muscle activity and more abduction and flexion of the shoulder and elbow joints.

To evaluate the capacity of UE mobility activities, the Brooke scale is used in most studies. As it is well standardized, it is more conducive to inter-study comparisons. Although widely used, the Brooke scale may not be sufficiently sensitive to measure differences in UE capacity in slowly progressive neuromuscular diseases [33]. Indeed, several studies have reported a decline of only one grade per decade [20, 27]. Relatively few subjects had a Brooke score of 5 or 6, which is consistent with clinical findings of problems with the proximal UEs only. Besides, the Brooke scale only classifies capacity of basic reaching activities of the arm and hand (ICF d4452). In the

study conducted by Mahjneh [22], a self-created six-stage scale was used to evaluate capacity of basic UE activities. However, most of the patients in this study were in stage 3 or 4, which suggests that this modified scale is probably also not sensitive enough to detect changes in the course of time. Specific measures to evaluate UE capacities such as the Jebsen test [35] or patient reported questionnaires such as the Abilhand [36, 37] and the Disabilities of Arm Schoulder and Hand (DASH) [38] have not been used. Also measures to evaluate performance of UE activities in daily life are lacking. Some studies have used the BI to assess capacity of self-care activities. This index is, however, very general and does not specifically assess activity limitations of the UEs. Stübgen [26] and Lue [18] reported a ceiling effect when using the BI to evaluate ADL in FSHD and LGMD patients. Measures that assess capacity of domestic life activities were lacking as well as measures that assess performance of self-care and domestic life activities.

A better understanding of UE impairments and activity limitations in patients with muscular dystrophies such as FSHD and LGMD is needed to evaluate rehabilitation interventions. Such understanding is also important for identifying the requirements for developing innovative arm-support devices to restore and/or enhance the performance of daily activities.

Study limitations

In current review, we found that some studies used the same subjects. In FSHD, the subjects of the study of Tawil et al. [14] were also used in the study of the FSH-DY group [13]. As for LGMD, the studies of Stübgen et al. [25–27] used the same group of subjects and also the studies of Lue et al. [17, 18, 21] have included some of the same subjects. Besides, no intervention studies were included to avoid a possible bias in describing the natural course of UE functions and activities. Some of these intervention studies may have included other measures to assess capacity or performance of UE activities other than the measures that are described in this article.

Conclusions and recommendations

This is the first overview of UE functions and activities in FSHD and LGMD. The clinical course of UE impairments and activity limitations associated with FSHD and LGMD is difficult to predict due to its high variability. An early age of disease onset may be associated with more severe disease progression. However, no clear correlation between strength, gender, age or duration of symptoms has yet been established. In general, FSHD and LGMD patients experience difficulty elevating their upper extremities and the execution of tasks takes considerably longer. Hand function largely remains intact. In the current review outcome measures to assess UE functions and activities in patients with FSHD and LGMD included MMT to evaluate muscle function and the Brooke Scale to evaluate UE capacity. There was however, a lack of specific outcome measures to assess UE function and UE capacity and performance in daily life. For additional and specific assessment of UE function, measures such as 3D motion analysis and EMG recordings are recommended. Questionnaires like the Abilhand are recommended to assess UE capacity and accelerometry to assess UE performance in daily life. Such measures may also be valuable to evaluate the effect of interventions such as training with or without the use of supportive devices.

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4

Upper limb function and activity in people with facioscapulohumeral muscular dystrophy: a web-based survey

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Abstract

Objective: To investigate the upper extremity (UE) at the level of impairments and related activity limitations and participation restrictions in people with facioscapulohumeral muscular dystrophy (FSHD).

Methods: The study was conducted using web-based questionnaires that were distributed amongst people with FSHD in the Netherlands. Eighty-eight respondents started the survey, and 71 completed it. The questionnaires covered the dimensions: Function, Activity and Participation of the International Classification of Functioning Disability and Health.

Results: More than 40% of the respondents experienced pain in one or both arms. Increased pain and stiffness scores and longer disease duration were associated with increased limitation scores. For basic activities, lifting the arm above shoulder-level was most frequently reported as most limited, coherent with the clinical picture of FSHD. Fifty percent of the respondents indicated restrictions at school, 78% at work and more than 80% indicated restrictions whilst participating in sports, hobbies, household activities and in romantic relationships.

Conclusions: This study has shown that alongside the well-known problem of lifting the arms above shoulder-level, UE activities below shoulder height during vocational and occupational activities are also problematic in patients with FSHD. Alongside disease duration, pain and stiffness are associated with UE activity limitations.

4.1 Introduction

Facioscapulohumeral dystrophy (FSHD) is an autosomal dominant, slowly progressive type of muscular dystrophy, with an estimated prevalence of 1:21,000 [1–3]. FSHD is, thus, one of the most common inherited muscular dystrophies with the first signs of weakness occurring in the muscles of the face and shoulder girdle [4]. Fatty infiltration with loss of muscle fibres gradually results in weakness of nearly all skeletal muscles [5]. Despite the typical pattern of muscle involvement described in the literature [6], the upper extremity (UE) impairments are highly variable among people with FSHD with regard to both proximal and distal muscle weakness [7, 8]. In addition, no clear correlations have been found between muscle strength and gender, age or duration of symptoms [9]. Although the clinical picture of muscle weakness is variable, most persons with FSHD experience activity limitations when elevating the arms above shoulder-level [10, 11]. It is also known that the execution of many activities of daily living (ADL) takes considerably longer in persons with FSHD compared to healthy subjects [8, 11]. Most people with FSHD are unable to raise their hands above their heads, but are able to bring their hands to their mouths. Hand function itself remains largely intact [9]. Interestingly, increased muscular co-contraction has been observed in the UEs of people with FSHD [5, 11], as well as enhanced electromyography activity in the shoulder muscles during arm elevation movements [11].

To develop tailored training interventions and new supportive aids, it is not only important to better understand UE impairments and limitations in basic UE activities, but also to obtain knowledge about limitations in more complex, instrumented UE activities and restrictions in social participation. Currently, little is known about the UE capacity and performance of daily activities in people with FSHD [9]. Hence, the aim of this study was to obtain a better understanding of the UE impairments and related limitations in activities and restrictions in participation in people with FSHD. In a previous study of boys and men with Duchenne Muscular Dystrophy (DMD), a web-based survey that consisted of a set of questionnaires covering all relevant dimensions of the International Classification of Functioning Disability and Health [12] was used. The same web-based survey was used in this study. Based on the

clinical picture of people with FSHD, it was hypothesised that especially activities above shoulder-level would be limited, but also that several participation restrictions would be present, independent of working above shoulder-level. In addition, it was hypothesised that UE activity limitations would be associated with disease duration, pain and stiffness.

4.2 Methods

Participants and procedure

A web-based survey (QuestionPro; Survey Analytics LLC, Seattle, USA) was designed. This survey included questions concerning pain and stiffness, as well as items to assess basic and daily (instrumented) UE activities. The survey was sent via the Dutch patient organisation, 'Spierziekten Nederland', to their Dutch-speaking members with FSHD in the Netherlands, in December 2011. The recruitment period was from December 2011 until February 2012. Ethical approval was obtained from the local Research Ethics Committee (Ethical Committee Arnhem-Nijmegen, 2008/341).

Outcomes

Outcomes were divided into four categories: (1) participant characteristics; (2) impairments; (3) activity limitations; and (4) participation restrictions.

Participant characteristics

The participant characteristics that were assessed were: age, age of diagnosis, disease duration, hand preference, wheelchair confinement and use of assistive devices for the arms. For the analyses, the originally-preferred arm was used.

Impairments

The questions on pain and stiffness were adapted from the University of Michigan Upper Extremity Questionnaire [3, 13]. Both pain and stiffness scores were divided into the aspects frequency (range: 0-6, with the higher the score, the higher the frequency), severity (range: 0-10, with the higher the score, the more severe) and disablement due to pain or stiffness (range: 0-10; with the higher the score, the more disabling). Combination scores were calculated for each part of the arm, by taking the sum of the three aspects (range: 0-26). A similar approach was used previously in the study of Janssen et al. [12]. Along with the scores for each segment of the arms, total sum scores for both the right and left UE were calculated (range: 0-182). For each segment, percentages of respondents that experienced pain and stiffness (combination score > 1) in either the right or left UE were determined.

Activity limitations

The Brooke scale [14] was used to classify UE activity, the Capabilities of Upper Extremity Questionnaire (CUE) [15] was used to assess basic UE activities and the ABILHAND-plus [16] to assess UE capacity to perform daily activities. The CUE contains 17 items (of which 15 one-handed, scored on both right and left arm and 2 two-handed), yielding in 32 scores with a seven-point scale (1 = unable to perform, 7 = can perform without difficulty). The CUE questionnaire in this study had 16 items in total, because the item 'hold a hammer' was missing. The ABILHAND-plus questionnaire contained 26 items (22 items that were described by Vandervelde et al. [16], and four additional items that were indicated as important by boys with DMD [12] that were scored on a three-point scale (0 = impossible, 1 = difficult, 2 = easy). Participants were also asked to select the five items that were most important to them and to report the activities in daily life that caused most problems due to UE impairments or activity limitations.

Participation restrictions

To assess the level of participation, a set of open questions was used. Respondents were asked if they went to school, had a job, practiced sports, had hobbies, participated in household activities, performed activities with friends and/or were in a romantic

relationship. Respondents who reported that they participated in a specific role, were asked if they were restricted due to UE impairments or activity limitations.

Statistical analysis

The mean and standard deviation was calculated for age, age of diagnosis and disease duration. Because not all data were normally distributed, we used non-parametric statistics. The median and inter-quartile ranges (IQR) of the pain and stiffness combination scores and of the Brooke, CUE total, CUE right/left and ABILHAND-plus scores were determined. Moreover, the percentages of respondents that reported a CUE activity to be very, extremely, or totally limited, the percentages of respondents that reported an ABILHAND-plus activity to be difficult or impossible, and the percentage of respondents that mentioned an ABILHAND-plus activity as important were calculated. Answers to the open question “What are the most important problems you encounter in daily life due to limitations in your arms and/or hands?” were categorised. The activities that restricted the performance of specific social roles were determined and categorised for each of these roles.

Wilcoxon signed rank tests were used to compare differences in pain, stiffness and CUE scores between the right and left UEs and between the preferred and non-preferred UEs. Spearman rho correlation coefficients of the pain, stiffness, Brooke, CUE and ABILHAND-plus scores with disease duration and age were calculated, as well as Spearman rho correlation coefficients of CUE and ABILHAND-plus scores with the Brooke scale. Finally, backward multivariate linear regression analyses were performed to determine the effect of disease duration (in years), pain and stiffness on basic arm activities measured with the CUE. All statistical analyses were carried out using IBM SPSS Statistics Version 20 for Windows (IBM®, Somers, USA). If a participant did not fully complete the survey, all completed items were included in the analysis.

4.3 Results

Participant characteristics A total of 88 respondents began the survey, of whom, 71 (81%) completed it. As a result, the number of respondents varied between the different domains of the questionnaires (see tables). The mean age of all respondents (N=88) was 51.1±14.8 years, the mean age of diagnosis was 32.0±16.0 years and the mean disease duration was 19.1±13.1 years. The percentage of participants with FSHD that were completely wheelchair confined was 17.6%. The same percentage (17.6%) of participants used some form of arm support.

Impairments

Seventy-one participants (81%) were right-handed. Ten participants (11%) reported that they switched their preferred arm (nine from right to left, and one from left to right). The median pain and stiffness scores of the right UE were generally higher than of the left UE. However, these differences were far from statistically significant for the shoulder and arm (P>0.5). For the wrist (p=0.04), thumb (p=0.06) and fingers (p=0.08) the differences were (nearly) significant. The overall pain combination score was significantly higher for the right arm (p=0.03). The overall stiffness combination score did not reach statistical significance for the left-right-difference (p=0.06). When the preferred arm was considered, no significant differences were found between the summed pain and stiffness scores of both arms (respectively p=0.25 and p=0.31). Pain was most severe in the shoulders and upper arms. The percentage of respondents that experienced pain (combination score higher > 1) in one or both arms varied between 43.9% and 89.0% percent for the different segments (Table 1). The overall pain score correlated with disease duration (rs=-0.28, p=0.01), but not with age (rs =-0.09, p=0.45). Stiffness was also most severe in the shoulders and upper arms. The percentage of respondents that experienced stiffness in one or both arms varied between 40.3% and 66.2% percent for the different segments (Table 1). No significant correlations were found between stiffness scores and disease duration or age.

Table 1: Pain and stiffness scores (range 0–26) of various upper extremity segments, as reported by people with FSHD.

Pain	N	Combination scores (median right arm / median left arm)	Respondents who experienced pain[a] (%right arm / %left arm)
Shoulders	80	11.0 / 10.0 (p=0.67)	89.0 / 82.9
Upper arms	80	9.0 / 7.5 (p=0.52)	74.4 / 73.2
Elbows	80	1.5 / 0.0 (p=0.78)	51.2 / 43.9
Forearms	80	3.0 / 3.0 (p=0.58)	58.5 / 52.4
Wrists	80	4.0 / 3.0 (p=0.04)	57.3 / 54.9
Thumbs	80	1.5 / 0.0 (p=0.06)	50.0 / 43.9
Fingers	80	2.0 / 0.0 (p=0.08)	51.2 / 46.3
Whole arm	80	39.0 / 31.5 (p=0.03)	
Stiffness	N	Combination scores (median right arm / median left arm)	Respondents who experienced stiffness[b] (%right arm / %left arm)
Shoulders	75	9.0 / 9.0 (p=0.51)	66.2 / 64.9
Upper arms	75	6.0 / 6.0 (p=0.39)	58.4 / 59.7
Elbows	75	0.0 / 0.0 (p=0.25)	40.3 / 40.3
Forearms	75	0.0 / 1.0 (p=0.60)	45.5 / 45.5
Wrists	75	2.0 / 1.0 (p=0.11)	50.6 / 46.8
Thumbs	75	2.0 / 1.0 (p=0.04)	50.6 / 48.1
Fingers	75	2.0 / 1.0 (p=0.13)	50.6 / 49.4
Whole arm	75	35.0 / 31.0 (p=0.06)	

[a]Pain combination score >1
[b]Stiffness combination score >1

Activity limitations

The median Brooke scale was 2 (IQR 2-3). The Brooke scale ($rs = 0.43$, $p<0.01$) and the CUE score ($rs=-0.37$, $p<0.01$) correlated with disease duration, but there was no correlation between disease duration and the ABILHAND-plus sum score ($rs=-0.11$, $p=0.35$). No significant correlations between Brooke, CUE and ABILHAND-plus scores for age were found. The Brooke scale significantly correlated with the CUE score ($rs=-0.48$, $p<0.01$) and the ABILHAND-plus score ($rs=-0.31$, $p<0.01$).

The median CUE total score was 155.5 (IQR 117.8-176.3), which was 70% of the maximum possible score. The median of both the CUE right and CUE left score was 75.0 (73% of the maximum possible score). Wilcoxon Signed-Ranks Tests indicated that the CUE right score was significantly lower than the CUE left score ($p=0.02$) and that the CUE score of the preferred arm was lower compared to the non-preferred arm ($p=0.03$) (Table 2). However, the medians of the CUE right/left scores as well as the CUE preferred/non-preferred scores were equal, indicating a minimal scale of the difference. The percentage of respondents that reported CUE activities being very, extremely or totally limited was higher for the items considering the right arm as for the left arm items.

The median ABILHAND-plus sum score was 44.0 (IQR 35.0-50.5), which was 84% of the maximum possible score. The three activities that were most often indicated as difficult were ‘buttoning up a shirt’ (56%), ‘taking the cap of a bottle off’ (47%) and ‘fastening the zipper of a jacket’ (44%). The three activities that were most often reported as important were ‘using the keyboard of a computer’ (66%), ‘using a knife and fork” (52%) and ‘fastening the zipper of a jacket’ (45%) (Table 2).

Multivariate regression analysis for the right arm revealed that the time since diagnosis, pain and stiffness explained 34% of the variance of the CUE. For the left arm these factors explained 40% of the variance. Table 3 shows that for both arms, pain, stiffness, and disease duration were all independently associated with limitations in basic UE activities as assessed with the CUE.

The answers to the open questions revealed that reaching for and lifting of objects above shoulder level caused most problems, followed by personal care and carrying objects (Table 4).

Table 2: Upper extremity activity limitations measured with the CUE and ABILHAND-plus, as reported by people with FSHD.

	N	Median (IQR)	
Brooke scale	76	3 (2-3)	
CUE score total (max score = 210)	74	155.5 (117.8-176.3)	
CUE score right (max score = 98)	74	75.0 (55.5-84.0)	
CUE score left (max score = 98)	74	75.0 (59.5-85.0)	
CUE score both (max score = 14)	74	6.0 (3.8-8.3)	
ABILHAND-plus score (max score = 52)	73	44.0 (35.0-50.5)	
CUE	N	% respondents that answered the activity to be very, extremely or totally limited (right / left / both arms)	
Reach forward at shoulder-level	74	41.9 / 36.5 / *	
Arms over head	74	79.7 / 73.0 / *	
Reach to the floor	74	39.2 / 36.5 / *	
Raise a five pound object over the head	74	* / * / 62.2	
Slide a light object towards you	74	10.8 / 9.5 / *	
Slide a ten pound object towards you	74	40.5 / 37.8 / *	
Slide a light object away from you	74	12.2 / 8.1 / *	
Slide a ten pound object away from you	74	37.8 / 29.7 / *	
Push up in chair	74	* / * / 58.1	
Curl wrist upward	74	18.9 / 13.5 / *	
Supination	74	14.9 / 8.1 / *	
Hold a hammer			
Pick up a small object with thumb and first two fingers	74	14.9 / 10.8 / *	
Hold a small object between thumb and index finger	74	13.5 / 8.1 / *	
Hold/open a two pound object with the tips of the fingers	74	25.7 / 20.3 / *	
Manipulate a small object with the fingers	74	17.6 / 12.2 / *	
Push a button with tip of the index finger	74	9.5 / 5.4 / *	
ABILHAND-plus	N	Difficult or impossible (%)[a]	Important (%)[b]
Take the cap off a bottle	73	46.6	24.7
Cut nails	73	38.4	21.9
Button up a shirt	73	56.2	38.4
Fasten the zipper of a jacket	73	43.8	45.2
Turn a key in a keyhole	73	21.9	37.0
Fasten a snap e.g. from jacket or bag	73	32.9	16.4
Open a pack of chips	73	31.5	2.7
Open a pack of biscuits	73	31.5	5.5
Insert a key in keyhole	73	20.5	41.1
Turn off a tap	73	21.9	35.6
Turn on a tap	73	21.9	37.0
Fill a glass with water	73	17.8	19.2
Sharpen a pencil	73	17.8	2.7
Open a lunch box	73	21.9	4.1
Squeeze toothpaste onto a toothbrush	73	15.1	20.5
Spread butter on a slice of bread	73	17.8	37.0
Open a toothpaste tube	73	21.9	12.3
Count banknotes	73	20.5	8.2
Handing out cards	73	28.8	8.2
Unwrap a chocolate bar	73	16.4	4.1
Dry hands	73	15.1	17.8
Wash hands	73	16.4	32.9
Eat with a spoon	73	28.8	27.4
Use knife and fork	73	38.4	52.1
Drink a glass of water without straw	73	24.7	42.5
Use keyboard of a computer	73	27.4	65.8

ABILHAND-plus=measure to assess UE capacity to perform daily activities, Brooke scale=measure to classify UE activity, CUE=measure to assess basic UE activities, IQR=Inter Quartile Range, *=not applicable.
[a] Percentage of respondents who answered the activity to be difficult or impossible.
[b] Percentage of respondents who identified the activity to be important. Respondents were asked to identify the five most important activities.

Table 3: Variables independently associated with limitations in basic upper extremity activities as assessed with the CUE based on linear multivariate regression analyses.

	Beta	Standard error	P value	95% CI
CUE Right arm[a]				
Duration	-0.67	0.15	<0.01	-0.98 – -0.36
Pain right	-0.14	0.06	0.03	-0.27 – -0.02
Stiffness right	-0.10	0.05	0.07	-0.21 – 0.01
CUE Left arm[b]				
Duration	-0.63	0.13	<0.01	-0.90 – -0.37
Pain left	-0.16	0.06	0.01	-0.27 – -0.05
Stiffness left	-0.09	0.05	0.07	-0.19 – 0.01

[a] R^2=0.34
[b] R^2=0.40

Table 4: Most limited upper extremity activities as reported by people with FSHD (N=73)

	%[a]
Reach / lift objects above shoulder level	45
Personal care activities	32
Carry objects	26
Eat / drink	19
Get dressed	19
Prepare food / household tasks	12
Using the computer / use telephone / write	11
Open cans / bottles	7
Use the toilet	3

Percentages of respondents who mentioned the activity when asking the open question "What are the most important problems you encounter in daily life due to limitations in arms and/or hands?"

Participation restrictions

Table 5 shows the percentage of respondents that reported participation restrictions, as well as the UE activities they experienced as most limited within different participation domains. Of all respondents, 11% went to school, 51% had a job or did voluntary work, 30% participated in sports, 94% had a hobby, 75% participated in household activities, and 81% had a romantic relationship. Fifty percent of the respondents indicated restrictions at school and 78 percent reported restrictions at work. More than 80% indicated restrictions, whilst participating in sports, hobbies, household activities and in romantic relationships. Carrying study materials, using a computer and household activities above shoulder height, (such as cleaning windows and hanging laundry) were specific activities that were reported as limited in at least 25% of the participants, who were involved in respectively school, work and household activities.

4.4 Discussion

To the best of the researchers' knowledge, this is the first study to explore upper extremity (UE) pain, stiffness, activity limitations and related participation restrictions in people with facioscapulohumeral muscular dystrophy (FSHD) [9]. The most important result is the frequent presence of pain and stiffness in the shoulders and upper arms, which was associated with UE activity limitations as assessed with the CUE. Besides pain and stiffness, time since diagnosis was independently associated with basic UE activity limitations. Together, these factors explained a substantial amount of the CUE variance (34-40%). The top three activities that were most often reported as being limited were: 'use of computer keyboard', 'use of knife and fork', and 'fastening zipper of jacket'. Half of the respondents indicated restricted participation at school in relation to UE activity limitations, 78% indicated restrictions at work and more than 80% whilst participating in other social roles.

With regard to pain and stiffness, it is well known that reaching upwards causes increasing difficulty in people with FSHD, when muscle weakness progresses [9, 10]. The most often applied strategy is making a ballistic movement of the arm, by means of the trunk muscles, through which the arm is 'thrown upwards'. This rapid compensatory

Table 5: Participation restrictions related to specific upper extremity activity limitations as reported by people with FSHD

Participation domain	%[a]	%[b]	Activities most often reported as limited	N	%[c]
School	11.0	50.0	Carrying study materials	2	25
(N= 73)			Typing	1	13
			Writing	1	13
Work	50.7	78.4	Using computer	13	35
(N= 73)			Writing	8	22
			Carrying	6	16
			Reaching high	5	14
			Other activities	4	11
Sports	30.1	86.4	Cycling	5	23
(N= 73)			Swimming	2	9
			Physical therapy / fitness	2	9
			Other activities	10	45
Hobbies	94.4	80.9	Sports / physical exercise	16	24
(N= 72)			Crafts	7	10
			Gardening	6	9
			Using computer	6	9
			Playing piano	5	7
			Photographing	5	7
			Other activities	9	13
Household	75.0	92.6	Window cleaning / hanging laundry	16	30
(N= 72)			Ironing / dish washing	6	11
			Vacuuming / mopping	5	9
			Carrying	4	7
			Other activities	29	54
In romantic relationship	80.6	81.0	Walking	14	24
(N= 72)			Shopping	11	19
			Entertainment / travel	10	17
			Sexuality	4	7
			Other activities	20	34

[a] Percentage of respondents that participated in this social domain,

[b] Percentage of respondents that suffered from upper extremity activity limitations, whilst participating in this social domain,

[c] Percentage of the respondents participating in this social domain that experienced upper extremity activity limitations in specific items.

movement may easily lead to overburdening or even micro-damage of structures in and around the shoulder, which in turn, may explain the pain and/or stiffness scores of this body segments.

A difference was found between the right and left arm with regard to the prevalence of pain complaints (medians 39.0 vs 31.5, p=.003). Because the majority of people is right-handed, this right/left difference may be explained by slight overuse of the right arm. When arm preference was however considered, no side difference between the pain scores was found when comparing the preferred and non-preferred arm. This could indicate an asymmetric involvement of the disease that is independent from arm preference. This would be consistent with the results presented by Rijken et al., who demonstrated more fatty infiltration on the right body side compared to the left independent of arm preference, in 70 patients with FSHD, using computed tomography (CT) scans [6]. The presented results did not show a clear side difference in limitations of basic activities (measured with the CUE).

Activities, such as sliding an object over a table and manipulating a light object with the fingers, were less difficult, probably, because these types of activities make less use of proximal muscles. However, a striking finding was the large percentage of participants that reported difficulties with desk-based activities, such as writing or using a computer. One explanation for this finding may be that the participants performed these activities without proper ergonomic positioning, whilst using their weakened arm and shoulder muscles too much. Another explanation could be that these activities are often performed over a longer time period, inducing muscle fatigue. Both explanations would support a rehabilitation strategy, in which the arms are supported by (adaptive) arm supporting devices during desk-based activities.

Both the Brooke and the CUE score were moderately ($r_s = 0.43$ and $r_s = -0.37$, respectively) correlated with disease duration. This is to be expected, as both scales assess the ability to lift the arms, which is a major problem for many persons with FSHD. In contrast, no correlation was found between the disease duration and the ABILHAND-plus. This can be explained by the fact that most activities assessed by the ABILHAND-plus involve a combination of arm and hand use, in which people can apply compensation strategies in order to succeed. It is also possible that the ABILHAND-plus is less sensitive to ‘minor’ activity limitations than the CUE, since the CUE contains questions aiming at basic activities with the arm or hand only. At the

impairment level, only pain was associated with disease duration, but this association was only weak (rs = -0.28), suggesting a more indirect relationship between pain and progression of muscle weakness.

The mean age was 51 years, which clarifies that a low percentage of the respondents indicated going to school (11%) and a higher percentage indicated having work (51%). The total percentage of respondents who indicated participation in either school or work was 62%. It is possible that some respondents don't participate in a given domain at all due to limitations, although they would like to. In fact, it's likely that they are most restricted. The actual percentage of restrictions may therefore be higher than presented in this study.

Study limitations

81% of all respondents that started the survey, also completed the survey which may have caused bias. Since the questionnaire was send not only by email, but also via a link in a public digital newsletter, it is unknown how many persons received the invitation. This may also have caused bias. Such response bias may have obscured the experiences of either more severely or less severely affected persons. Moreover, the results of this study are based on a survey among the Dutch population with FSHD. Because the standards of care are relatively high in the Netherlands, generalisation of these results to FSHD patients in other countries requires caution. Another limitation of this study is that the gender distribution of the respondents remained unknown. The applied questionnaire was originally designed for people with DMD. Since DMD is extremely rare in women, gender was not questioned. Erroneously, this adjustment was not corrected in the current study. The results of this study provide little information about young persons with FSHD. Both the mean age of the study sample and the mean age of diagnosis were relatively high compared to other studies (Bergsma, Cup et al. 2014). Only one participant was younger than 18 years. One explanation could be that children and teenagers do not yet experience severe UE activity limitations or do not want to be confronted with these limitations by participating in this survey.

Recommendations

For future studies in patients with FSHD, a set of measures including the Brooke classification, pain and stiffness questionnaires and the CUE are recommended. In addition, a patient-centred participation scale, such as the Canadian Occupational Performance Measure (COPM) should be considered, to provide more insight in patient specific limitations. To evaluate the effects of individually tailored exercises and supportive devices, objective measures are recommended, that provide also quantitative kinematic and electromyography parameters. Such measures include e.g. 3D-kinematic movement analysis [17] and the use of accelerometry to assess actual motor performance activities in daily life [18].

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5

Upper Extremity Kinematics and Muscle Activation Patterns in Subjects With Facioscapulohumeral Dystrophy

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Abstract

Objective: The aim of this study was to compare FSHD subjects with healthy controls during the performance of standardized UE tasks.

Methods: Eleven subjects with FSHD and eight healthy controls were measured. Kinematic data were recorded using a 3-dimensional motion capturing system. Muscle activities, recorded using electromyography, were obtained from 6 superficial muscles around the glenohumeral joint. Shoulder elevation and elbow flexion angles, and maximum electromyographic activity during the movements as a percentage of maximum voluntary contraction (MVC) were calculated.

Results: Kinematic differences between the FSHD group and the healthy control group were found in the shoulder elevation angle during single shoulder movements and both reaching tasks. In general, subjects with FSHD had higher percentages of muscle activation. The median activity of the trapezius was close to the MVC activity during the single shoulder movements. Moreover, deltoid and pectoralis muscles were also highly active.

Conclusions: Higher activation of the trapezius in subjects with FSHD indicates a mechanism that could help relieve impaired shoulder muscles during arm elevation around shoulder height. Compared with healthy subjects, persons with FSHD activated their shoulder muscles to a greater extent during movements that required arm elevation.

5.1 Introduction

Muscular dystrophies, although varying in type and severity, are more or less progressive and disabling in time [1]. Some forms of muscular dystrophy become symptomatic in infancy or childhood, whereas others do not become symptomatic until middle age or later. Facioscapulohumeral dystrophy (FSHD) is an autosomal dominant, slowly progressive type of muscular dystrophy. It is one of the most common inherited muscular dystrophies, with an estimated prevalence of 1:21,000 [2, 3]. In FSHD, the first signs of weakness are in the muscles of the face and shoulder girdle [4, 5]. Weakness of the shoulder girdle muscles results in impairment of arm function, including movements above shoulder level [5] and limitations in performing daily activities [6]. When persons have weakened shoulder girdle muscles and move their arms to carry out daily tasks, contraction of the relatively spared shoulder girdle muscles results in protraction and medial rotation of the scapula. The inferior angle of the scapula tends to rotate medially and the scapula separates from the ribcage. This so-called scapular winging is most apparent in UE abduction, but can be also found in UE forward flexion [7]. When healthy subjects achieve full range of shoulder motion, upward rotation and elevation of the scapula takes place [8, 9]. In contrast to healthy subjects, persons with FSHD cannot rotate the scapula laterally and are therefore unable to achieve full range of shoulder motion. Furthermore, because of a decreased acromiohumeral space, there is an increased risk of impingement.

Persons with FSHD have an increased impingement risk due to the use of compensatory movements, such as ballistic movements, in order to lift the upper arm and overcome the lack of strength of the scapular stabilizing muscles and ultimately to rotate the scapula. Innovative arm supports may help persons with FSHD to perform arm activities that would cost considerable effort or possible damage. In order to develop such support systems, knowledge of UE kinematics and muscle activity in FSHD is needed.

Several studies have focused on quantifying UE movements with different techniques. Basic arm function in FSHD has often been quantified using the Brooke scale [10–13],

which is an observational scale ranging from 1 to 6 (a higher score indicates more limitation in arm function). More specific knowledge concerning muscle activity is confined mainly to manual muscle testing (MMT) of muscle groups during performance of joint movements such as elbow flexion [6, 10, 12, 13]. Some studies present MMT scores of muscle groups instead of overall scores only [10]. However, the strength of an individual muscle can hardly be measured, and using MMT provides very limited knowledge on the coordination between muscles. Coordination of UE muscles during reaching tasks has mostly been studied in healthy elderly persons [14, 15] and those who have experienced a stroke [16, 17]. Only one study to date has described UE kinematics and muscle activation in FSHD [18]. In that study, the movement and muscle activity of the biceps brachii, triceps and deltoid of a group of persons with FSHD were described during a simulated drinking task and were compared with a group of healthy controls. The pattern of muscle activity and movement in the FSHD group during the simulated drinking task involved more co-contraction of muscles and more abduction and flexion of the shoulder and elbow joints compared to the movement pattern of healthy controls(14). Electromyography (EMG) activity as a percentage of the maximum voluntary contraction (%MVC) was also higher in the FSHD group compared to healthy controls. Bakhtiary et al. [18] also hypothesized that individuals with FSHD have fewer intact muscle fibers and will therefore recruit a higher percentage of the remaining muscle fibers to perform tasks. The study of Bakhtiary et al. [18] provided the first knowledge of the arm function in FSHD during one daily task. However, muscles that are responsible for stabilizing the scapula were not investigated. The aim of the current study is to gain a deeper understanding of shoulder and elbow movements in FSHD. The purpose is to investigate the kinematics of the UE and the involvement of specific proximal muscles during singular joint movements, reaching tasks and gross motor tasks in persons with FSHD and healthy controls.

5.2 Method

Participants

Eleven persons with FSHD (four male, seven female, mean age 33.9±11.5, 10 right dominant, one left dominant) and eight healthy volunteers (five male, three female,

Table 1: Tasks that were executed by the participants

Movement	Instructions	Start position	End position
Single joint movements			
Shoulder abduction-adduction	Move the arm sideward/upwards as far as possible and move the arm back to the start position. Keep the arms straight and the hand palm facing forward.		
Shoulder flexion-extension	Move the arm forward/upward as far as possible, then bring the arm back to the start position. Keep the arm straight, with the hand palm facing inward.		
Reaching tasks			
Reach up ipsilateral • Active protraction scapula	Reach toward the target at shoulder height on the ipsilateral side.		
Reach up contralateral • Active protraction scapula	Reach toward the target at shoulder height and 1 shoulder width on the contralateral side.		
Gross motor tasks			
Bring the hand to the mouth • Active flexion • Active supination • Passive pronation	Bring the fingers of the hand to the mouth and back to the start position onthe table top. Wrist about 20cm in front of abdomen.		
Pushing-pulling	Push the object as far as possible forward from the starting position withoutmoving the chest and then pull it back. Use the lateral edge of the object as reference to follow a line on the table put at 1 shoulder width from themiddle.		

NOTE. Not all participants were wheelchair bound; the figures are intended only for illustrative purposes.

mean age 49.9±9.8, all right dominant) participated in the study. The dominant side was tested in all persons. All persons gave written informed consent. None of the healthy participants had a history of musculoskeletal or neurological problems. Persons with FSHD were recruited by an invitation letter from the Dutch patient organization of persons with muscle diseases (Spierziekten Nederland). All persons with FSHD scored a 2-3 score on the Brooke scale [19], which meant that they were able to raise a 250 ml glass of water to the mouth. Subjects were excluded if they had suffered from previous upper limb trauma (e.g. bone fractures or surgery). Ethical approval was obtained for the study (Ethical Committee Arnhem-Nijmegen, NL39024.091.11), and the study was conducted in accordance with guidelines of the Helsinki protocol.

Table 2: MVC starting positions and instructions

Muscle	Start Position	Instruction
Biceps brachii	90°elbow flexion, palm facing upward. Examiner takes the hand and provides resistance to resist elbow joint flexion.	Flex the elbow as hard as possible, against the examiner's hand.
Deltoid (lateral part)	45°of shoulder abduction and extended elbow. The examiner holds the arm and resists abduction of the shoulder.	Abduct the arm against the force generated by the examiner's hand.
Triceps brachii	90°elbow flexion and 90°abduction. The examiner supports the elbow and holds the wrist, to resist elbow joint extension.	Extend the elbow against the examiner's hand.
Trapezius (upper part)	Arms hanging vertically beside the trunk. The examiner's hands are placed on top of the shoulders, to prevent upper arm elevation.	Elevate both shoulders, against the examiner's hands.
Pectoralis major (clavicular part)	Upper arm abducted 90°and the elbow flexed in 90°. One hand of the examiner supports the forearm, while the other hand is used to resist adduction and flexion of the shoulder in the horizontal plane.	Flex the upper arm against the hand of the examiner at the upper arm.
Latissimus dorsi	90°shoulder abduction, 90°elbow flexion, and external rotation of the upper arm. One hand of the examiner supports the elbow to resist adduction of the shoulder, while the other hand is used to keep the wrist in position.	Adduct the upper arm.

Data recording

All assessments were performed using a standardized protocol at a motion analysis laboratory (Maastricht University, The Netherlands). The movements were recorded with an eight Vicon MX camera system (Oxford Metrics Group, UK) operating at a frequency of 200 Hz, and the data were filtered using spline-interpolation (Woltring, 1995). Reflective markers were attached on the subject's body following the guidelines of the Upper Limb model [20] (Figure 1). Because the scapula rotates underneath the skin, it is hard to detect rotation and tilting of the scapula with this method.

The movement protocol consisted of two single joint movements (shoulder abduction-adduction [SAA] and shoulder flexion-extension [SFE]), two forward reaching tasks at shoulder level (to the ipsilateral side [RFUI] and contralateral side [RFUC]) and two gross motor tasks (hand to mouth and pulling/pushing of an object on a table). EMG data from the biceps brachii, deltoid (lateral part), triceps brachii, trapezius (upper part), pectoralis major (clavicular part) and latissimus dorsi (important during UE adduction [21]) muscles were collected with Delsys Trigno sensors operating at 2 kHz. The serratus is also important for coordinated UE movements and scapula stabilization. The serratus muscle, as being composed of several bellies, can however not be measured reliably using this method of bipolar surface electrodes, and was left out of this protocol. Sensors were attached following the guidelines by SENIAM [22]

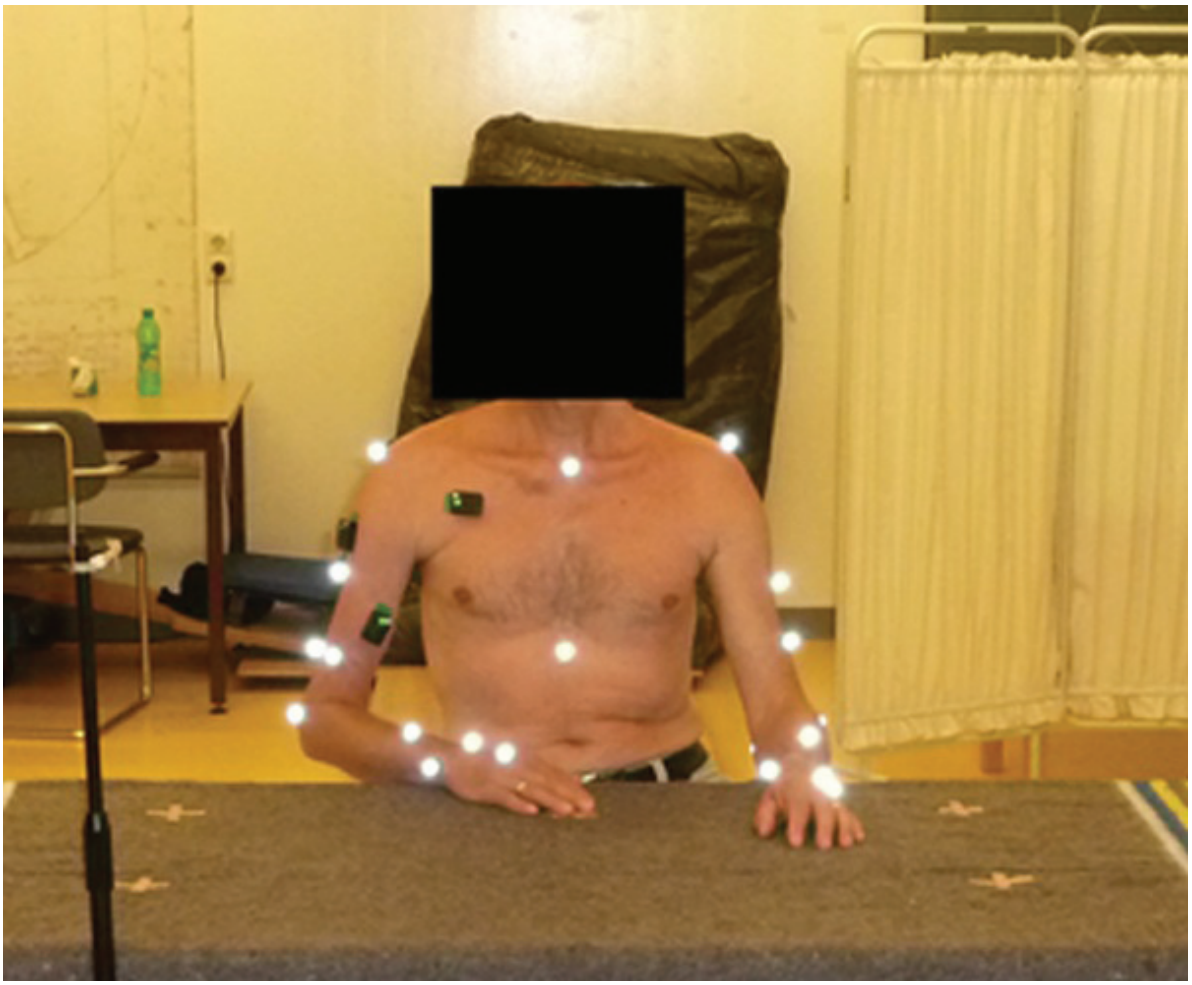

Figure 1: Marker setup for unassisted movements

and Delagi et al. [23]. The skin was prepared by shaving the skin surface if needed and cleaning the skin with alcohol. Each task consisted of three repetitions of the same movement with a common start and endpoint, and at self-selected speed. Each of the healthy participants was asked to sit on a height-adjustable chair without a backrest. During the reaching and the gross motor tasks, a table was also placed in front of the subject. When the table was used, the height of the chair was adjusted until the elbow angle was 90º with the hand resting on the table and the upper arm in a vertical position (Figure 1). The target for the reaching tasks was placed at arm length and one shoulder width on the ipsilateral or contralateral side at shoulder level. In the SAA and SFE tasks, the subject was instructed to complete the task up to his/her maximum voluntary active range of motion. The starting point for the hand in the reaching tasks and the hand to the mouth movement was on the table at the subject's mid-line and about 20 cm from the abdomen. Table 1 summarizes the tasks.

Before execution of the set of movements, participants were asked to perform MVCs to record the maximum EMG activity for each of the six muscles. The EMG activities of the muscles were recorded during 3 s of isometric MVC, and each test was performed twice for each muscle. During execution of the MVCs, the subject was encouraged verbally to produce the maximal contraction. The positions in which the MVC were performed are summarized in Table 2.

Data processing

Analysis of kinematic parameters

The joint angles were calculated using the Vicon Upper Limb model. For each person and each task, the mean of the maximum upper-arm elevation and minimum and maximum elbow flexion angle of the three repetitions was calculated. Upper-arm elevation was used, because the clinical terms 'flexion' and 'abduction' can be confusing. Flexion followed by abduction would give different results than abduction followed by flexion [24]. Flexion is elevation parallel to the sagittal plane and abduction is elevation in the frontal plane. For both the control group and the FSHD group, the median values of maximum upper-arm elevation and minimum and maximum elbow flexion angle were calculated. The upper-arm elevation and elbow flexion angles were selected since they are most influenced by the effects of gravity and would thus require a greater muscle

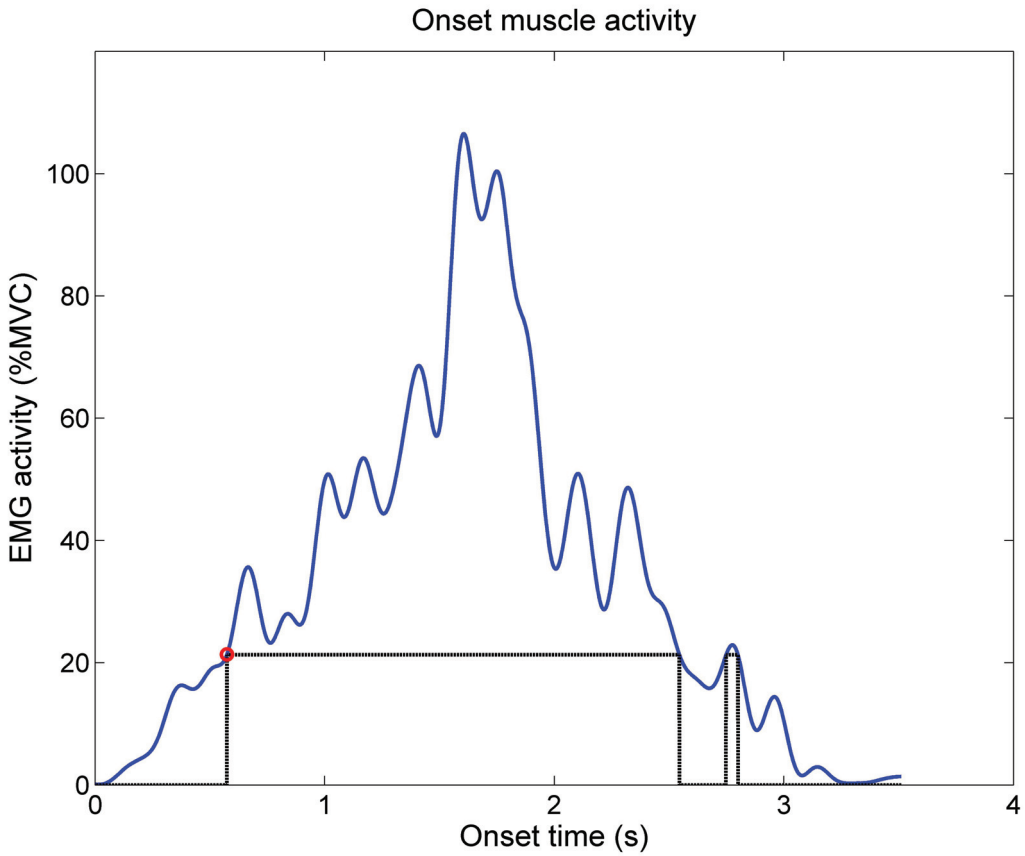

Figure 2: Onset time of the muscle activity. The continuous line represents an EMG signal and the dashed line indicates when the muscle activity was more than 20% of the maximum EMG value for a period of at least 0.2 s. The circle represents the point that is considered as onset time of the muscle activity.

activity to compensate for the weight of the arm. In order to avoid a confounding effect due to the starting and finishing of the movement, the second repetition of each task was used for further analysis. The movement of the hand marker was considered as the starting point. The duration of each movement was compared between the control group and the FSHD group.

EMG

The recorded EMG data were filtered with a fourth-order Butterworth bandpass filter from 20 to 450 Hz and then rectified. For each person and each muscle, a MVC norm value was calculated. This was defined as the maximum value of the rectified signal of

both MVC contractions. The %MVC of the activities was then expressed as the EMG signal divided by the MVC norm for the corresponding muscle. For each movement, muscle and person, the mean of the maximal %MVC of the three repetitions was calculated. Moreover, the muscle activation patterns were analyzed by comparing the onset times of the individual muscle contractions. For each task, the onset time of a muscle was calculated for the second repetition. The onset time was defined as the percentage of the duration of the movement where the EMG activity was higher than 20% of the maximum EMG value for a period of at least 0.2 s during that specific movement (Figure 2).

Statistics

The data were not normally distributed, so the median and interquartile ranges (IQRs) were used to describe the data. The non-parametric Wilcoxon rank-sum test was used to compare the medians between the FSHD group and the healthy control group for each task; the effect size was also calculated. The significance level was set at $\alpha = 0.05$.

5.3 Results

Only one person with FSHD was able to elevate the arm above 120º during the two single joint movements of SAA and SFE. All persons were able to complete the reaching tasks and the gross motor tasks. Three tasks (SAA, RFUI, RFUC) were performed significantly slower (completion time approximately 25 to 40% slower) by the FSHD group compared to the healthy control group. Table 3 gives the kinematic and EMG parameters recorded during execution of different tasks, from the FSHD and the control group.

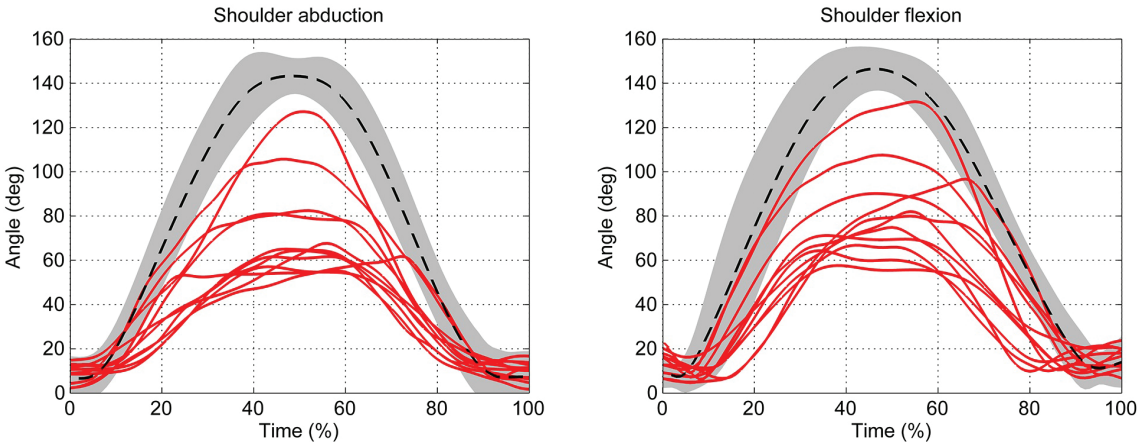

Figure 3: The data representing the maximum upper-arm elevation angle of shoulder abduction (left) and flexion (right). The grey band represents the 95% confidence interval of the control group, the dashed lines represent the average of the control group and the continuous lines represent the persons with FSHD.

Arm kinematics

The data depicted in Figure 3 represent the upper-arm elevation angles of the healthy control group and the FSHD group. Significant differences between the FSHD group and the healthy control group were found in the upper-arm elevation angle during SAA and SFE movements and during the two reaching tasks (Table 3). A larger variance was found in the maximum upper-arm elevation angle of the SAA and SFE movements in the FSHD group. In addition, the FSHD group showed less extension of the elbow during the contralateral reaching task (Figure 4 and Table 3). Significant differences were found in the duration of the shoulder abduction movement, the ipsilateral reaching task and the hand to the mouth task P=0.02, P=0.04 and P=0.01, respectively).

Muscle activation

On average, the maximum EMG activation as %MVC was significantly higher in the FSHD group than in the control group (Table 4, Figure 5). During the SAA movement, the trapezius activity in the FSHD group was significantly higher than that of the control group (respectively 115% and 35%). In addition, during the two reaching tasks, the maximum trapezius activity was also significantly higher in the FSHD group (median 59% and 47% of MVC in the FSHD group versus 10% and 13% in the control group).

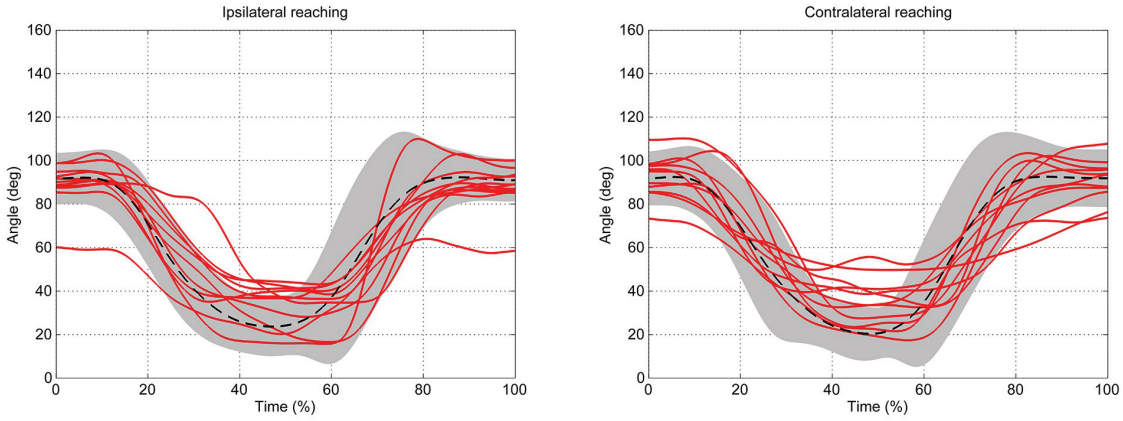

Figure 4: Elbow flexion angles during reaching tasks. The grey band represents the 95% confidence interval of the control group, the dashed lines represent the average of the control group and the continuous lines represent the persons with FSHD.

Compared to the healthy control group, in the FSHD group the maximum biceps brachii activity was significantly higher during SF movement and both reaching tasks, which included upper-arm elevation and flexion. Moreover, the maximum activity of the biceps during these movements was higher than during the hand to the mouth task. During the SFE movement and the reaching tasks, the maximum triceps activity was also significantly higher in the FSHD group. The maximum activity of the deltoid muscle was only significantly higher in the FSHD group compared to the control group during the ipsilateral reaching task and the hand to the mouth task. The maximum activity of the pectoralis was significantly higher in the FSHD group during all tasks. The maximum activity of the latissimus muscle was only significantly higher in the FSHD group during the hand to the mouth task. Visual inspection of the timing of muscle activation did not reveal any difference between the control group and the FSHD group.

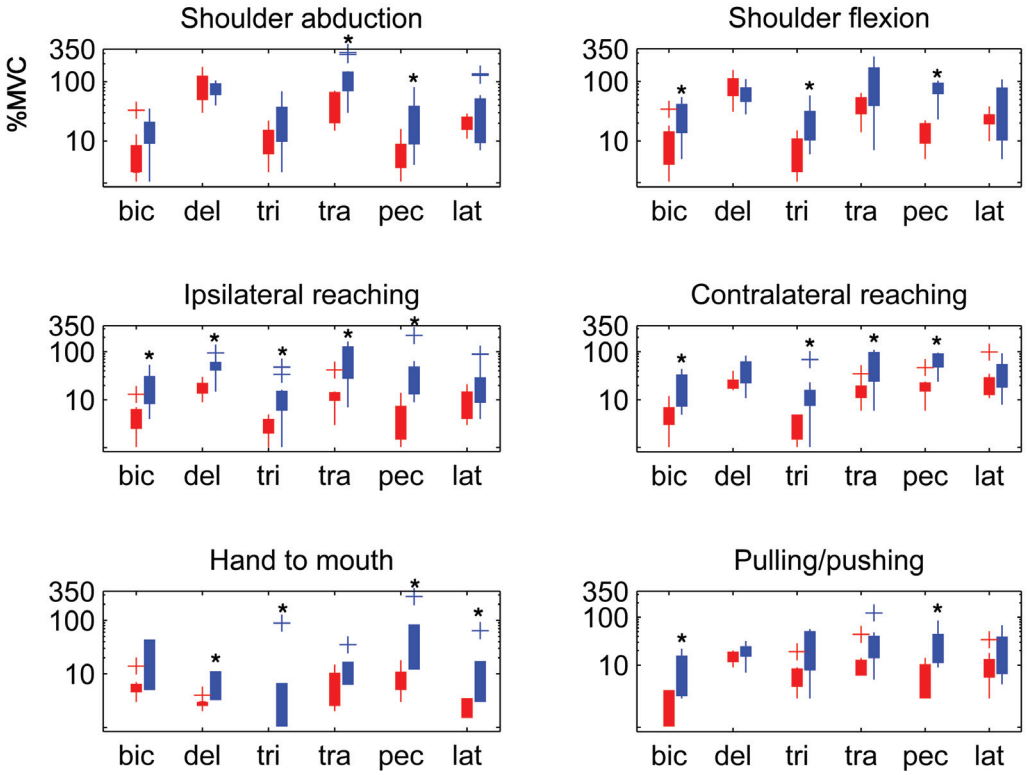

Figure 5: Boxplots of maximum muscle activation as %MVC during performance of predefined tasks. The red bars represent the IQRs of the muscle activity as %MVC on a logarithmic scale of the control group; the blue bars represent the IQRs of the FSHD group (bic=biceps brachii, del=deltoid, tri=triceps brachii, tra=trapezius, pec=pectoralis major, lat=latissimus dorsi). Plusses represent outliers and asterisks represent comparisons that are significantly different.

Table 3: Maximum angles during execution of tasks

	Max upper arm elevation (º)		Max elbow flexion (º)		Min elbow flexion (º)		Duration (s)	
Task	Median	IQR	Median	IQR	Median	IQR	Median	IQR
SAA								
Control	144.9	141.0-145.9	38.7	35.3-44.4	22.6	21.4-27.9	3.8	3.2-5.3
FSHD	65.8 (P<0.01; r=-0.83)	60.5-81.3	41.2 (P=0.49; r=-0.17)	33.5-56.9	21.5 (P=0.60; r=-0.13)	19.9-33.5	5.6 (P=0.02; r=-0.54)	5.1-7.3
SFE								
Control	147.6	144.8-149.7	45.6	35.2-54.3	15.8	13.5-23.4	3.7	3.0-4.3
FSHD	81.6 (P<0.01; r=-0.83)	67.6-96.3	40.1 (P=0.54; r=-0.15)	27.6-53.3	16.4 (P=1.00; r=0.00)	13.5-22.2	4.7 (P=0.13; r=-0.36)	3.0-6.4
RFUI								
Control	83.8	78.0-90.6	98.5	93.2-100.9	20.6	17.3-30.7	2.4	2.1-2.7
FSHD	68.7 (P<0.01; r=-0.74)	66.2-77.1	94.0 (P=0.35; r=-0.23)	91.6-99.0	24.8 (P=0.24; r=-0.28)	16.6-34.8	3.2 (P<0.00; r=-0.63)	2.9-4.1
RFUC								
Control	85.6	84.3-93.9	95.7	92.8-105.9	18.6	13.4-23.7	2.4	2.2-2.8
FSHD	69.1 (P<0.01; r=-0.64)	67.1-83.2	96.3 (P=0.97; r=-0.02)	91.9-105.5	26.9 (P=0.01; r=-0.59)	21.1-38.2	3.2 (P=0.05; r=-0.46)	2.5-3.7
H2M								
Control	49.5	42.9-53.1	136.1	131.3-139.6	82.2	78.2-87.8	2.2	1.9-2.6
FSHD	46.2 (P=1.00; r=0.00)	42.4-59.7	134.5 (P=0.51; r=-0.16)	129.0-138.3	87.5 (P=0.17; r=-0.33)	82.9-94.2	3.8 (P=0.04; r=-0.47)	2.3-4.0
PP								
Control	69.5	63.6-74.4	94.4	92.1-104.4	17.1	14.3-20.2	3.9	3.1-4.2
FSHD	64.7 (P=0.15; r=-0.34)	58.7-68.8	100.3 (P=0.21; r=-0.30)	97.0-105.9	13.2 (P=0.21; r=-0.30)	10.6-23.9	4.7 (P=0.08; r=-0.42)	3.4-5.7

NOTE. Differences between control and FSHD group tested with Wilcoxon rank-sum test; P values and effect sizes are shown in parentheses. Abbreviations: H2M, hand to the mouth; IQR, interquartile range; Max, maximum; Min, minimum; PP, pushing/pulling; RFUC, reach up contralateral; RFUI, reach up ipsilateral.

Table 4: Maximum electromyographic activation during execution of tasks

	Max EMG											
	Biceps (%MVC)		Deltoid (%MVC)		Triceps (%MVC)		Trapezius (%MVC)		Pectoralis (%MVC)		Latissimus (%MVC)	
Task	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR
SAA												
Control	3	3 - 11	60	45 - 144	11	5 - 16	35	18 - 68	5	3 - 9	21	15 - 26
FSHD	16	8 - 22	85	59 - 95	20	8 - 38	115	68 - 149	28	8 - 40	16	9 - 59
	(p=0.05; r=-0.46)		(p=0.72; r=-0.10)		(p=0.09; r=-0.40)		(p<0.01; r=-0.64)		(p=0.01; r=-0.57)		(p=0.66; r=-0.11)	
SFE												
Control	5	3 - 16	69	55 - 122	8	3 - 11	40	25 - 57	16	7 - 20	23	18 - 29
FSHD	27	13 - 46	56	45 - 83	17	10 - 36	95	30 - 182	69	61 - 98	23	7 - 92
	(p=0.02; r=-0.55)		(p=0.27; r=-0.27)		(p=0.01; r=-0.57)		(p=0.06; r=-0.44)		(p<0.01; r=-0.83)		(p=0.84; r=-0.06)	
RFUI												
Control	4	3 - 7	18	13 - 23	3	2 - 4	10	9 - 15	3	2 - 8	7	4 - 16
FSHD	14	7 - 32	52	40 - 64	10	6 - 16	59	21 - 141	29	13 - 54	18	8 - 32
	(p<0.01; r=-0.63)		(p<0.01; r=-0.68)		(p<0.01; r=-0.70)		(p<0.01; r=-0.66)		(p<0.01; r=-0.74)		(p=0.11; r=-0.38)	
RFUC												
Control	4	2 - 8	22	17 - 27	4	1 - 5	13	11 - 22	20	14 - 24	20	12 - 33
FSHD	14	7 - 34	51	21 - 65	11	7 - 16	47	20 - 101	81	45 - 92	26	18 - 57
	(p<0.01; r=-0.63)		(p=0.05; r=-0.46)		(p<0.01; r=-0.72)		(p=0.01; r=-0.59)		(p<0.01; r=-0.78)		(p=0.66; r=-0.11)	
H2M												
Control	6	4 - 7	3	2 - 3	1	0 - 1	6	3 - 12	8	4 - 11	3	2 - 4
FSHD	6	5 - 51	6	4 - 12	2	1 - 7	7	6 - 20	23	14 - 101	7	3 - 22
	(p=0.15; r=-0.35)		(p<0.01; r=-0.65)		(p=0.02; r=-0.53)		(p=0.24; r=-0.29)		(p<0.01; r=-0.67)		(p=0.02; r=-0.53)	
PP												
Control	1	1 - 4	17	11 - 19	6	3 - 9	8	6 - 13	4	2 - 11	6	5 - 16
FSHD	5	2 - 17	23	15 - 25	23	6 - 55	32	11 - 43	16	11 - 47	16	6 - 44
	(p=0.01; r=-0.61)		(p=0.24; r=-0.28)		(p=0.05; r=-0.46)		(p=0.05; r=-0.46)		(p<0.01; r=-0.64)		(p=0.15; r=-0.34)	

NOTE. Differences between control and FSHD group tested with Wilcoxon rank-sum test; P values and effect sizes are shown in parentheses. Abbreviations: EMG, electromyography; H2M, hand to the mouth; IQR, interquartile range; Max, maximum; PP, pushing/pulling; RFUC, reach up contralateral; RFUI, reach up ipsilateral.

5.4 Discussion

The aim of this study was to gain a deeper understanding of shoulder and elbow movements and the shoulder muscle activation during single joint movements, reaching tasks and gross motor tasks in persons with FSHD. The main differences in the kinematics were found in the upper-arm elevation angles, which were smaller in the FSHD group during shoulder abduction and flexion movements and the two reaching tasks. Only two FSHD subjects were able to lift their arm to about 90º during shoulder abduction and flexion. This is in line with the clinical picture of persons with FSHD. Persons with FSHD also presented much higher muscle activity during task performance in all six muscles that were investigated. The highest activity as %MVC was present in the trapezius.

In order to understand the findings, it is useful to differentiate between two phases occurring during shoulder abduction and/or flexion. A first phase includes arm elevation between 0 to 90º; in a second phase, this occurs from 90º and beyond. During the first phase, the deltoid muscle initiates upper-arm elevation together with other scapulohumeral muscles [25]. The maximal deltoid activity was shown to be lower in the FSHD group than in the control group for the SAA and SFE tasks. However, this result could have been induced by the greater arm elevation achieved by the healthy controls, although a possible sparing of the deltoid muscle to avoid undesired movements of the scapula could not be ruled out and should be further investigated. When axioscapular muscles such as the serratus anterior and trapezius cannot stabilize the scapula, contraction of the deltoid muscle may not only elevate the humerus but can also result in undesired movement of the scapula [25, 26].

This study hypothesized that the trapezius is highly active in FSHD in an attempt to rotate and elevate the scapula. In a healthy situation, the upper trapezius together with the lower trapezius and serratus anterior are responsible for stabilizing the scapula to the thoracic cage. The serratus anterior counterbalances the external moment around the sternoclavicular and acromioclavicular joints induced by the weight of the arm during UE abduction and flexion [21]. In addition, one of the most important functions of the trapezius occurs during the second phase of arm elevation from 90º and beyond when the trapezius is involved in rotating the scapula together with the serratus anterior [21, 25, 27]. Serratus anterior activity was not recorded in this study.

Inappropriate functioning of the serratus anterior muscle has however been mentioned as cause for scapular winging [26, 28, 29], a clinical symptom that is present in FSHD [26, 30]. Winging of the scapula results in lower acromion elevation, thus leading to a lower maximal elevation angle of the humerus [8]. The maximum %MVC activity of the trapezius was higher in FSHD subjects compared to healthy subjects and was even close to or higher than its activity during MVC during tasks where maximal UE elevation was required. This may indicate that the trapezius contributed to humeral elevation by rotating and elevating the scapula.

In the control group, the median biceps activity during movements that required upper-arm elevation was lower than during the hand to the mouth task. In the FSHD group, the opposite was observed, indicating that the biceps brachii muscle supports upper-arm elevation in FSHD. This is consistent with the biomechanical function of this muscle that, according to Itoi et al. [31], can also function as anterior stabilizer of the glenohumeral joint and thus assist in forward flexion of the shoulder joint [31]. Bakhtiary et al. [18] who studied the kinematics and EMG in FSHD during a simulated drinking task, found similar results. They concluded that the muscles around the shoulder and rotator cuff are weaker in FSHD and that the biceps is therefore recruited as an arm flexor. In present study, more tasks were investigated. The complex interaction between superficial shoulder muscles was evident in muscle-activation patterns that showed more co-contraction in the muscle activity in FSHD compared to healthy controls. During the reaching tasks, more co-contraction was present in the deltoid, trapezius, pectoralis and biceps brachii muscles. No difference in the starting time was found.

Study Limitations

Few methodological aspects can be considered as limitations of this study. The MVC was performed manually, while resistance was provided by one of the researchers. In some cases, it was difficult to immobilize the joints properly by hand. The maximum %MVC activity of the upper trapezius muscle during shoulder abduction and flexion was close to or higher than the EMG activity measured during MVC. It is known that reduced concentration, motivation and fear for or restrictions in the range of motion can influence a person's voluntary effort during MVC [32, 33]. It is possible that these factors influenced the performance of MVC in FSHD subjects and consequently

resulted in percentages above 100% of MVC during the execution of movements and tasks. Another explanation could be that differences exist between the EMG amplitude of maximal isometric contractions in MVC and the EMG amplitudes during maximal dynamic contractions. Bobbert et al. [34] have indicated that muscle activity during a maximal isometric contraction is smaller than during a maximal concentric contraction and EMG amplitude increases when movement velocity increases. Moreover, force measurements were not performed in this study. EMG data and 3D kinematics were recorded to study the movements of the arms in FSHD, and MVC was performed to indicate relative muscle activity for each of the six individual muscles. The relation between EMG activity and force produced has been extensively investigated in healthy subjects [35]. There may be consensus of the opinion that the EMG-force relationship is linear under isometric conditions and non-linear under isotonic conditions [35], although force prediction is still approximate at best. In contrast, the relationship between EMG and force in FSHD still has not been studied. It can be hypothesized that persons with FSHD have less normal working muscle fibers and that the maximum force they can produce is therefore reduced compared to healthy persons. To perform a certain activity, a minimum of force is needed that is comparable for healthy persons and persons with FSHD (for example to lift the weight of the arm). People with FSHD need to recruit a higher percentage of available muscle fibers to achieve the required force, resulting in a higher percentage of MVC. Although activity percentage indicates the required muscle effort to perform the movements, it provides no information about the exact forces generated.

Activity of the serratus anterior muscle, which is an important scapula stabilizer, was not recorded in this study. The reason for this omission is the limited accessibility of the serratus anterior by surface EMG. Another limitation was the sample size, which consisted of 11 FSHD subjects. However the study was explorative in nature and, despite the limited sample size, significant differences between movement patterns and muscle activities have been shown between healthy controls and FSHD subjects.

In order to further investigate muscle capacities, a combination of external force measurements, such as dynamometry, is recommended. Together with 3D motion characteristics and EMG, external force measurements this would provide a more complete understanding, because then the role of individual muscles can also be better estimated. The used method with surface EMG is not applicable for muscles that are not on the surface, like the rotator cuff muscles. The current investigation of six muscles

provided an initial understanding of the activities of the superficial shoulder muscles. However, the study was not focused on kinematic analysis of scapular movements and therefore does not provide a complete representation of the scapulohumeral motions. Investigating the involvement of rotator cuff muscles and deeper muscles such as the serratus anterior would require more invasive techniques such as fluoroscopy or intra-muscular needle EMG. As part of a complementary approach to understanding rotator cuff muscle contributions, biomechanical musculoskeletal models [21, 36, 37] could also be used.

As a long-term research perspective, it would be interesting to further evaluate whether the use of arm supports would result in more efficient movements that require less effort and would therefore enable the performance of tasks such as eating for longer periods of time. It could be hypothesized that arm supports would reduce the effort to perform movements during daily activities. In this study, the FSHD data were heterogeneous, implying that a one-size-fits-all approach may not be adequate but that a personalized approach would be needed to customize future arm supports. Understanding the effect of FSHD on muscle force and arm movements could help develop more biomechanically oriented assistive arm devices. Ideally, an arm support would counteract the gravity, thus allowing the users freedom to move their arm with limited effort. There are two different issues: 1) the problem of scapula control and the role of the serratus anterior and 2) the problem of UE weakness leading to muscle fatigue and impairments in performing daily tasks. For both problems an arm support would be helpful to enable persons with FSHD to perform daily tasks better. By counteracting gravity, less force is needed to lift the arm and thus less activation of the muscles, resulting in less fatigue. Further research is required in order to determine what the effect of arm support is on scapula control and fatigability.

Conclusions

This was the first study where the involvement of proximal, superficial scapulohumeral muscles during several standardized movement tasks in FSHD was explored and described. Compensations were found in FSHD subjects as a consequence of loss of muscle function; this resulted in increased muscle co-contraction and ultimately an increased effort and energy needed to accomplish tasks. The trapezius muscle was highly active in the shoulder abduction and flexion movements, indicating a mechanism

that compensates for the lack of scapular lateral rotation when the arm is elevated. Persons with FSHD used higher percentages of MVC in the weakened shoulder muscles during movements and tasks that required elevation in the shoulder joint. Further research should be focused on investigating whether existing arm-support systems reduce these muscular efforts, so that movements or tasks can be performed longer or more frequently.

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6

Effect of forearm gravity compensation on upper limb kinematics and muscle activation in persons with facioscapulohumeral dystrophy: A cross-sectional study

Murgia A., Bergsma A., Cup E. H., Groot I. J., Meijer K. Effect of forearm gravity compensation on upper limb kinematics and muscle activation in persons with facioscapulohumeral dystrophy: A cross-sectional study. **submitted**

Abstract

Objective: The aim of this study was to evaluate the effect of forearm gravity compensation, by comparing kinematics and muscle activity of participants with FSHD and healthy participants during standardized upper extremity tasks.

Methods: Eleven persons with FSHD and eight healthy controls were measured. Participants performed a series of upper extremity tasks without and with the aid of a forearm support mechanism (SLING). Kinematic data were recorded using a three-dimensional motion capture system. Muscle activities of six superficial muscles around the glenohumeral joint were recorded using surface electromyography. Shoulder elevation angles, maximum electromyographic activity and electromyographic activity onset during the movements (reaching tasks only) were calculated.

Results: Shoulder elevation angles differed in single joint tasks in the healthy group due to the mechanical design of the SLING. The elevation angle waveforms were otherwise similar between unsupported and SLING conditions within both groups. A decrease of muscle activity occurred in both groups when the SLING was used. In the FSHD group, later onsets of biceps and deltoid occurred in both SLING-assisted during ipsi- and contralateral reaching with the trapezius being also delayed during contralateral reaching. No temporal shifts were present in activation onsets in the deltoid-trapezius and deltoid-latissimus pairs between SLING and unsupported conditions.

Conclusions: Reduction of muscle activity can help relieve the load on the shoulder muscles during arm elevation around shoulder height. Changes in selected muscle onsets in the FSHD group could have implications for scapular mobility and stability, both of which should be considered when designing arm support devices for this group.

6.1 Introduction

Facioscapulohumeral dystrophy (FSHD) is one of the most common forms of muscular dystrophy [1–4]. It mainly affects the muscles of the face, the shoulder girdle and the upper arm. Common symptoms in the upper extremity are weakness of the shoulder girdle muscles, often associated with scapular instability, and of the upper arm muscles. This generally results in limitations while performing activities of daily living (ADLs) and in difficulties performing arm elevation [5]. In previous research, the time to complete daily tasks was often found to become considerably longer [6]. Moreover, in previous research it was found that persons with FSHD exhibited a higher activity of their shoulder muscles, especially of the trapezius, during movements that required humeral elevation at about shoulder level, when compared to healthy persons [7]. Arm elevation above shoulder height requires upward (lateral) rotation of the scapula [8] by the simultaneous action of the trapezius and the serratus anterior muscles [9]. Since the latter is greatly affected by the muscle dystrophy, it was hypothesized in a previous study that the higher activity of the trapezius could be also an indication of possible compensatory mechanisms aimed at overcoming limited scapular mobility [7].

An adequate form of arm support could, in principle, enable individuals with FSHD to overcome the limitations cited above. Support devices that compensate for arm weight have been extensively employed to assist persons with Upper Extremity (UE) impairments [10, 11]. Some of the simplest designs include those devices which use gravity compensation to relieve the weight of the upper extremity. In these devices, elastic elements, actuators or simple counterweights are used to balance the weight of the upper extremity. To be able to design more sophisticated arm support mechanisms, user-specific parameters such as muscle capacity and preferred activities, should be taken into account. The long-term outcome would be a more user-driven or personalized design process that adapts to the individual characteristics of each person. The effects of gravity compensation on UE kinematics and muscle activity have been studied before in healthy elderly [12, 13] and in persons with stroke [14] during reach and retrieval movements. Prange et al. [12] found that in the presence of gravity compensation, healthy elderly performed similar movements with a lower level

of muscle activity compared to the unsupported condition, while muscle activation patterns in terms of timing remained unchanged. Lower muscle activity was mainly found in the biceps, deltoid and trapezius muscles. Using the same gravity compensation device as in the study by Prange et al. [12], Coscia et al. [13] also reported unaltered upper limb kinematic synergies and muscle activation patterns in healthy persons being assisted during reaching with different levels of arm support. Similar results were also found in stroke persons performing reaching with and without the aid of a gravity compensation device [15].

Although the effect on UE kinematics and muscle activity resulting from the use of an arm support are well-investigated in healthy elderly and in persons with stroke, there is still a lack of evidence on the changes induced by arm supports in person with neuromuscular dystrophies who have compromised shoulder function, for example FSHD, and could greatly benefit from this assistive technology. It would be particularly relevant in order to design adaptive support systems to understand whether kinematics and electromyography (EMG) activity is changed in persons with FSHD as result of using an arm weight support system. Such information could be useful when designing arm support systems which provide an optimal level of support by adapting to the changing dynamics of the user during a specific movement. The aim of the current study was to investigate how UE kinematics and shoulder muscle activities are influenced by gravity compensation in persons with FSHD compared to healthy controls. Changes in shoulder kinematics and muscle activity were quantified while participants performed a set of standardized tasks with and without gravity compensation. It was hypothesized that performing tasks with gravity compensation would result in changes in individual muscle onset times in FHSD persons, because the mechanism would compensate for the function of the already weak shoulder muscles.

6.2 Methods

Participants

Eleven persons with FSHD (mean age 49.9 ± 9.8 yrs, four men, seven women, 10 right dominant, one left dominant) and eight healthy persons (mean age 33.9 ± 11.5

yrs, five men, three women, all right dominant) were tested on their dominant side. None of the healthy participants presented musculoskeletal or neurological problems. FSHD participants were recruited through the Dutch patient organization of persons with muscle diseases (Spierziekten Nederland).

All FSHD participants had a score of 2 or 3 on the self-assessed Brooke scale [16], meaning they were able to raise a 250 ml glass of water to the mouth. Participants were excluded if they had suffered from previous upper limb trauma (e.g. bone fractures or surgery). Ethical approval was obtained for the study (Ethical Committee Arnhem-Nijmegen, NL39024.091.11) and the study was conducted in accordance with the guidelines of the Helsinki protocol.

Data recording

Participants were asked to perform a set of standardized movements [7], first without assistance and then while being assisted by a passive gravity support mechanism (SLING arm support, Focal Meditech BV, The Netherlands). The SLING is constructed so that counterweights can be added to a slider, which can vertically move inside a support column (black cylinder Figure 1) and is connected through a cable to the forearm support. The total cable tension is the sum of the weight of the slider plus the weight of the counterweight, which can be customized. The total vertical cable tension was chosen for each person so that he/she experienced a weight-free upper extremity.

The movement protocol consisted of two shoulder movements: abduction-adduction (SAA) and flexion-extension (SFE); two reaching tasks at shoulder level: reaching to the ipsilateral (RFUI) and to the contralateral side (RFUC); two gross motor tasks: hand to mouth (H2M) and pulling/pushing of an object on a table (PP). The data of the movements without the SLING were described in a previous study [7]. Movements were recorded with an 8 camera Vicon MX system sampling at 200 Hz (Vicon Motion Systems Ltd. UK). Reflective markers were attached to the subject's UE and trunk (Figure 1), following the guidelines of the upper limb model [17].

Participants were asked to repeat each task three times at self-selected speed in a cyclic fashion, while they were sitting sit on a height-adjustable chair without a

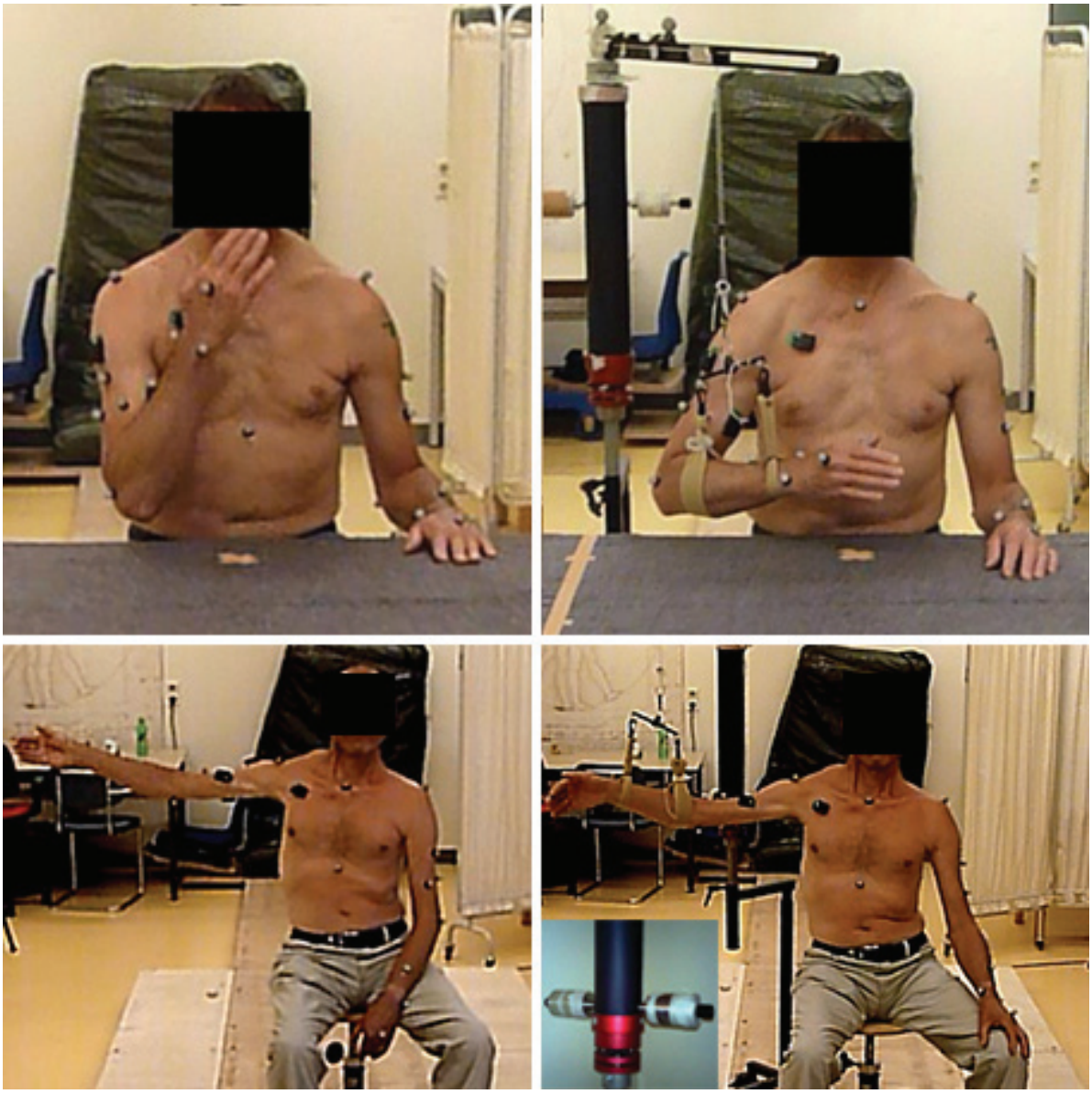

Figure 1: Left: marker setup for unassisted movements. Right: marker setup for SLING assisted movements. Inset bottom right: detail of the counterweights plates that can be removed or added to change the amount of tension on the cable.

backrest. During the reaching and the gross motor tasks, a table was placed in front of the participant. The height of the chair was adjusted so that an elbow angle of 90º was formed between the upper arm in a vertical position and the forearm when the hand was placed on the table. For each task, a common start and endpoint was defined and participants were instructed to complete each task up to his/her maximum possible active range of motion. The starting position for the shoulder movements was the arm hanging alongside the body. The starting position for the hand to the mouth movement and the reaching tasks was with the hand on the table, on the subject's mid-line and distant about 20 cm from the abdomen. For the reaching tasks, a target was placed at shoulder level, at arm length and one shoulder width to the ipsilateral or contralateral side.

EMG data were collected with Delsys Trigno (Delsys Inc. USA) sensors sampling at 2 kHz for six muscles that are involved in shoulder and upper arm movements: biceps brachii, deltoid (lateral part), triceps brachii (long head), trapezius (upper part), pectoralis major (clavicular part) and latissimus dorsi muscles. Sensors were attached following international guidelines [18, 19]. In order to normalize the EMG data, participants were asked to perform isometric maximum voluntary contractions (MVC) against the manual resistance exerted by one of the investigators to record the maximum EMG activity for each of the six muscles before the tasks were performed. For each muscle, the MVC test was performed twice, while the EMG activity was recorded for 3 s [7]. An alternative normalization to the division by MVC, which used the z-scores, was also implemented as described below.

Data processing

Marker data were filtered using Woltring spline-interpolation (predicted MSE value=15) [20] and the Vicon Upper Limb model was used to calculate the joint angles. For each task and each person, the starting point of a movement (defined as the moment when the vertical coordinate of the hand marker started moving) was determined visually. Similarly the end point of the movement was defined as the point when the hand stopped moving after returning to the common start point once the target was reached. From the kinematics of each movement, the maximum and minimum shoulder elevation and elbow flexion angles were determined. The active range of motion (AROM) was calculated using the difference between the maximum and minimum angles. For

both the control and FSHD group, median values for the shoulder elevation and the elbow flexion angles were calculated for the movements with and without the SLING support. In order to check whether trunk movements were different between healthy controls and FSHD participants, the maximal Euclidean distance of the marker that was attached to the top of the sternum on the jugular notch, was calculated between the start and end of the first repetition. EMG data were bandpass filtered (4th order Butterworth: cutoff 20 - 450 Hz) and rectified using a root mean square algorithm. The EMG data were normalized as percentage of MVC (%MVC) per person and muscle. The MVC norm value was defined as the maximum value of the rectified signal from both MVC contractions. Each task was repeated three times and for each repetition, the %MVC values of the highest amplitude were calculated. The mean of the maximum %MVC values of the repetitions was then calculated for each task, each muscle and each person. As an alternative to the normalization approach using MVC, a normalization analysis was conducted by transforming the rectified EMG values to z-scores [21, 22]. The z-score for each trial and each muscle were computed for each subject, using the EMG mean and standard deviation values of the unsupported (no-SLING) condition. The normalization to z-scores was performed to reduce the influence of potentially unreliable MVC values, among muscles and across subjects, and to eliminate differences of tonic EMG values. For the two reaching tasks, the EMG was selected in the interval between the moment when the hand marker started moving (0%) and the moment when it stopped moving at the end of the movement (100%). Within this interval the onset time was defined as the time corresponding to the muscles exceeding an activity threshold of 5 standard deviations (SD) of the EMG during a quiet period. In other research [7] a threshold value equal to 20% of the maximum EMG value has been proposed. This value would be related to a substantial muscle activation that has a functional effect. However in order to quantify the exact moment when an EMG signal starts to increase significantly from the noise background level, a 5·SD threshold was used here (Figure 2) [23]. The two reaching tasks were chosen as being representative of a subject's abilities, since their execution requires significant active range of motion and values of the shoulder joint moments near their maximum. These tasks have also been investigated by other researchers on healthy persons and stroke patients [12–14].

Beside the onset times, the shoulder elevation angle relative increase between the start of the movement and the time of onset was calculated for each muscle. This outcome parameter was chosen to quantify at which specific shoulder elevation angle any given

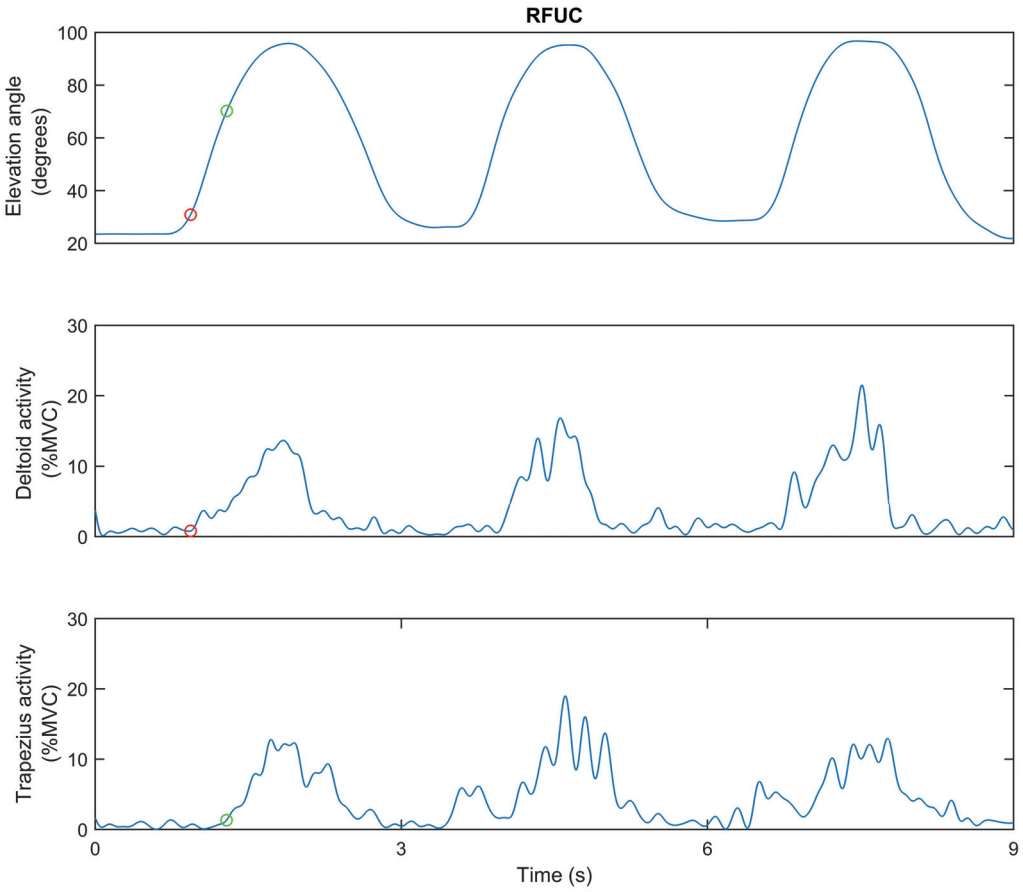

Figure 2: Example of how EMG onset and corresponding angles were determined for one participant of the control group during the RFUC task. The shoulder elevation angle and the activities of the deltoid and trapezius muscles are shown from top to bottom, respectively.

muscle became active with respect to the start of the movement. It was chosen as an additional quantification of the muscle onset changes that may be induced by the SLING. In addition to the onset time and the corresponding increase in shoulder elevation angle, the relative difference between onset times of deltoid-latissimus dorsi and deltoid-trapezius muscles as percentage of normalized time was calculated for the two conditions with and without the SLING. These muscle groups were considered because of their involvement during arm elevation (deltoid, trapezius) [9] and their role in glenohumeral head stabilization through the counteraction of upwards and downwards forces (deltoid, latissimus dorsi) [24].

Statistics

Non-parametric statics were used to analyze the data since these were not normally distributed. The median and interquartile ranges (IQR) were used in the descriptive statistics. Wilcoxon signed-rank tests were used to compare the kinematic data, maximum and minimum muscle activity, the relative muscle onset times and corresponding increases in shoulder elevation angle between the start of the movement and the time of onset between the two conditions with and without the SLING, for both the FSHD group and the control group. In addition, the shoulder elevation angle waveforms during the movements with and without the SLING were compared for each subject and each task. This was done by calculating the coefficient of multiple correlation (CMC), as described by Kadaba et al. [25], between the shoulder elevation angles that were normalized in time of a specific movement performed with and without the SLING. The CMC was calculated using the between-days formula where the two days were the conditions with and without the SLING [26]. This provides information on the similarities in shape of the shoulder elevation angle waveforms. The significance level for all statistics was set at α = 0.05.

6.3 Results

Kinematics

The kinematic data are summarized in Figure 3. Higher maximum shoulder elevation angles resulting from SLING-support were found in reaching and H2M movements in the FSHD group, and in the H2M movements in the healthy persons ($P<0.05$). The shoulder elevation angles were lower in SAA and SFE movements when the SLING was used by healthy persons. The minimal shoulder elevation angle was higher ($P<0.05$) in all SLING-assisted movements in the FSHD group compared to the non-assisted conditions. Moreover, execution time was shorter during the SLING-assisted shoulder and H2M movements compared to the condition with no SLING ($P<0.05$ only for SAA), but longer in the SLING-assisted reaching and PP tasks ($P<0.05$ only in RFUC). Movement of the trunk decreased when the SLING was used during the SFE movement, in both the control and the FSHD group ($P<0.05$, median reduction 27 mm in the control group and 25 mm in the FSHD group). For the H2M, the trunk movement increased ($P<0.05$, median increment 4 mm in control group and 3 mm in FSHD group). An increment in trunk movement was found for the FSHD group compared to the control group for the unsupported SAA, H2M and RFUI and the supported SFE movement. The maximum difference was 19 mm. The CMC values for the shoulder elevation angle waveforms with and without the SLING were above 0.83 for the SAA, SFE, RFUI, RFUC, PP movements and above 0.54 for the H2M movement.

Muscle activation

In general, muscle activity was lower for all muscles during the SLING-assisted movements compared to the unsupported movements (Figure 4). The results of the analysis of the EMG data normalized as %MVC were qualitatively the same as those using the z-scores. In the FSHD group the maximum EMG activity of each of the measured muscles, except for the latissimus dorsi (MVC and z-score normalization) and the pectoralis (z-score normalization only), were lower ($P<0.05$) in the SLING-assisted shoulder movements (SL SAA and SL SFE) compared to the unsupported movements. In this same group, the activities of all muscles were also lower during the SLING-

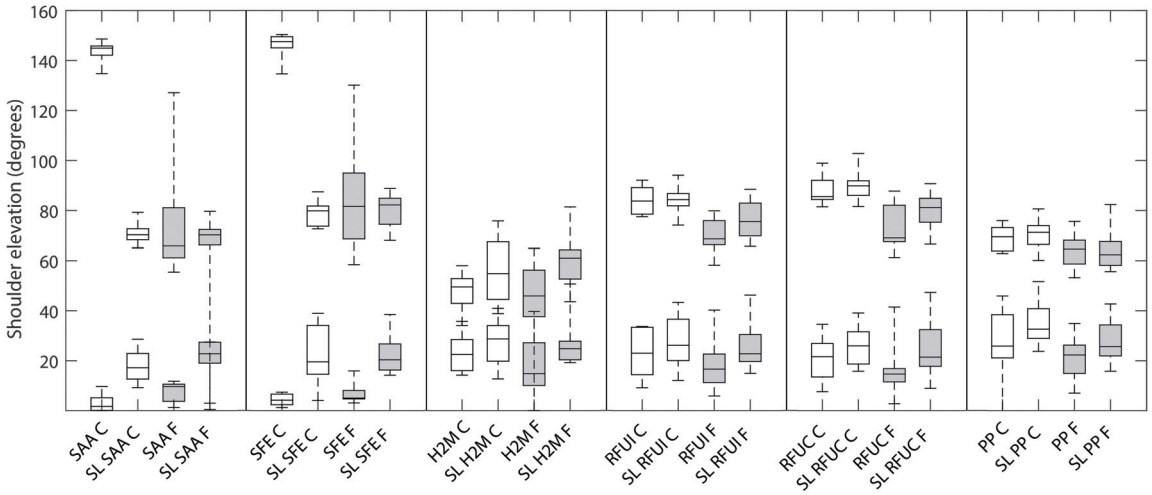

Figure 3: Boxplots showing maximum and minimum shoulder elevation angles during execution of various tasks in healthy controls (white boxes) and persons with FSHD (grey boxes) without and with the SLING (SL). The median value is represented by the horizontal line within the box.

assisted RFUC task ($P<0.05$). During the SLING-assisted RFUI task the activities of all muscles were lower except for the triceps (MVC and z-score normalization) and the latissimus (z-score normalization). In the SLING-assisted H2M the activity of the pectoralis was lower ($P<0.05$; MVC normalization) and during the SLING-assisted PP movement the activities of the biceps, deltoid and triceps were lower ($P<0.05$) as well as that of the pectoralis ($P<0.05$; z-score normalization only). In the healthy control group during the SLING-assisted RFUC movement, the biceps and deltoid became active later ($P<0.05$) than in the unsupported condition, the biceps also became active later in SLING RFUI movement ($P<0.05$). In the FSHD group, the onset of the biceps and deltoid occurred later ($P<0.05$) in both SLING-assisted RFUI and RFUC tasks, with the trapezius' onset also occurring later in the RFUC movement ($P<0.05$). The activity of trapezius and deltoid muscles in relation to the shoulder elevation angle appeared to show a prominent increase in activity near the maximum reached elevation angle in selected FSHD cases (see Figure 5). This was visible in both unassisted and assisted movements.

Concerning the relative increase in shoulder elevation angle between the beginning of the movement and the moment when a muscle became active: only the deltoid in the healthy participants became active at a higher angle ($P<0.05$) during SLING

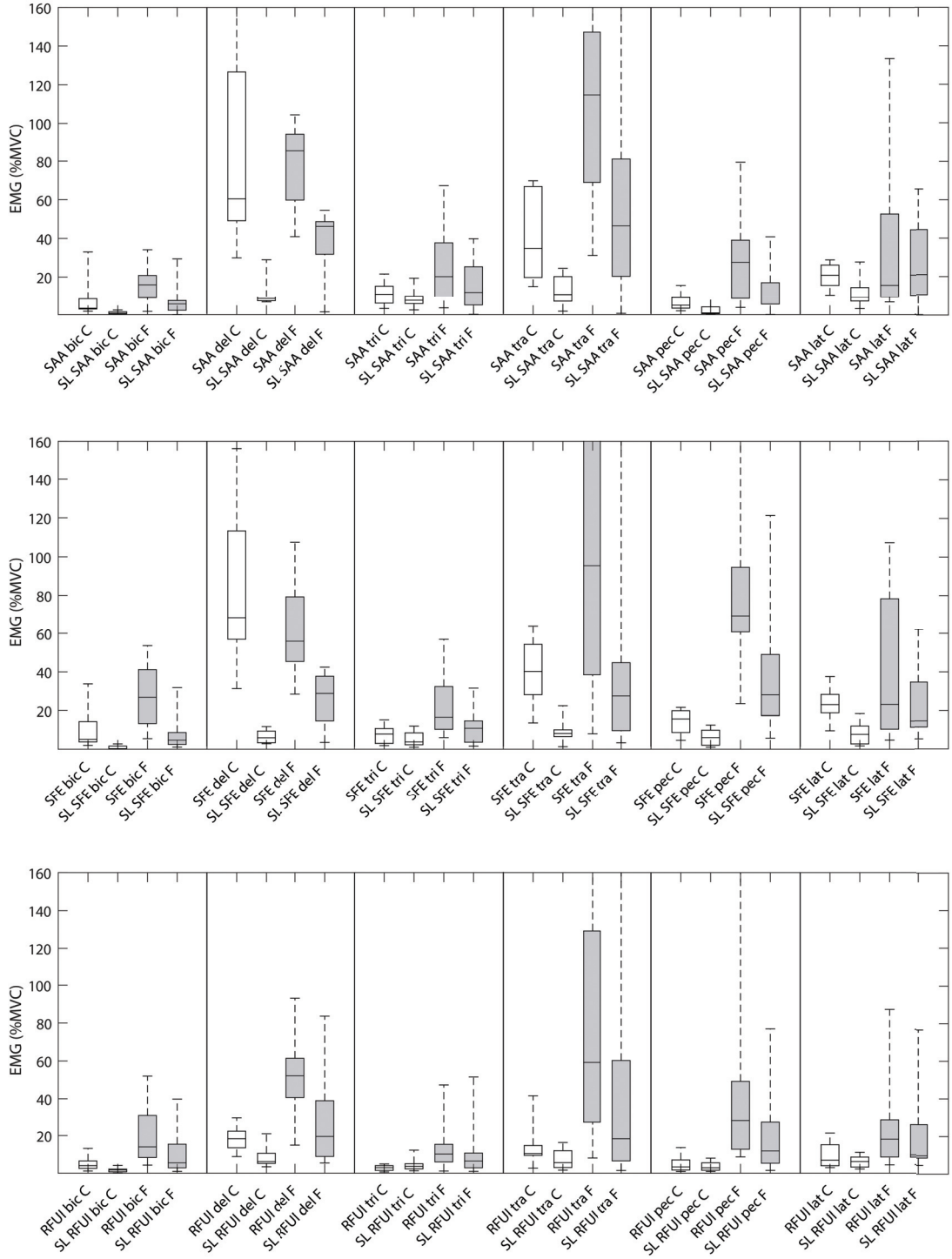

Figure 4: Boxplots showing maximum EMG activation as percentage MVC during execution of various tasks (SAA, SFE, RFUI) in healthy controls (white boxes) and persons with FSHD (grey boxes) for all muscles without and with the SLING (SL). Bic: biceps; Del: deltoid; Tri: triceps; Tra: trapezius; Pec: pectoralis; Lat: latissimus dorsi. The median value is represented by the horizontal line within the box.

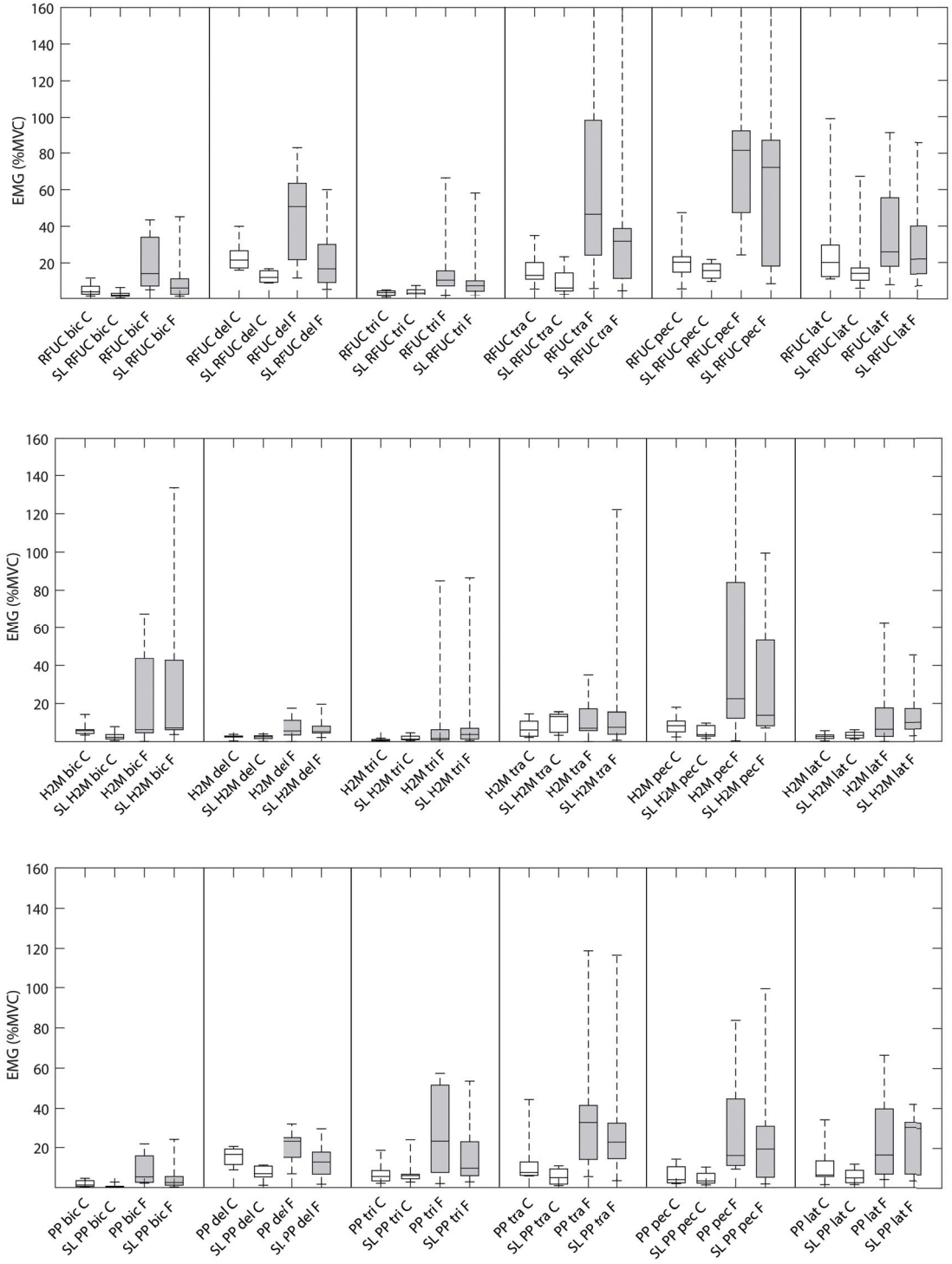

Figure 5: Boxplots showing maximum EMG activation as percentage MVC during execution of various tasks (RFUC, H2M, PP) in healthy controls (white boxes) and persons with FSHD (grey boxes) for all muscles without and with the SLING (SL). Bic: biceps; Del: deltoid; Tri: triceps; Tra: trapezius; Pec: pectoralis; Lat: latissimus dorsi. The median value is represented by the horizontal line within the box.

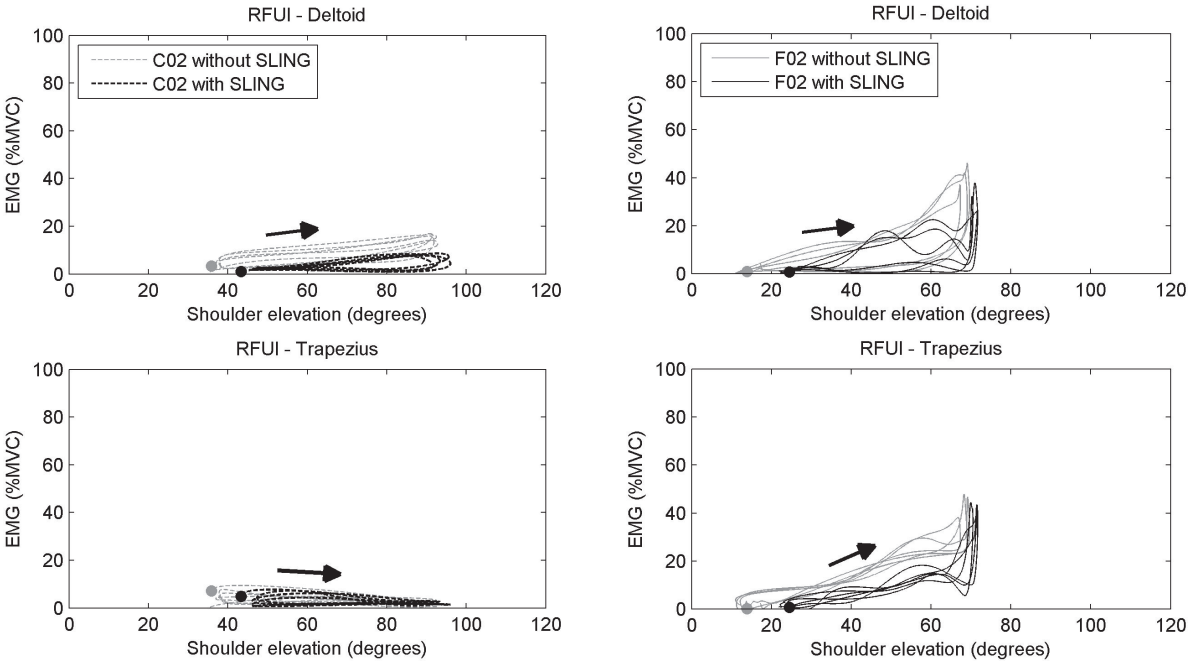

Figure 6: Activity of deltoid and trapezius versus shoulder elevation angle during reaching tasks for participant C02 (control group) and participant F02 (FSHD group). The filled circle and the arrow indicate the beginning of the movement and its direction respectively.

RFUC, while in the FSHD group biceps, deltoid and trapezius became all active at a higher angle ($P<0.05$) during SLING RFUC. In addition to the differences in onset times between the SLING and unsupported conditions for each individual muscle, the differences between the deltoid-trapezius and deltoid-latissimus dorsi muscle pairs were also considered during the two reaching tasks. None of the relative onsets (deltoid-trapezius and deltoid-latissimus) changed as result of the SLING in both reaching tasks ($P>0.05$).

6.4 Discussion

This is the first study that is aimed at quantifying the influences of arm gravity support on joint kinematics and muscle activity in persons with FSHD and healthy persons, when performing a set of standardized tasks encountered in daily life. A reduced maximal muscle activity in all tasks was generally observed in addition to muscle onset changes during the reaching tasks in both groups.

Concerning the kinematic changes resulting from the introduction of the arm support, or SLING, the angular waveforms for shoulder elevation were in general qualitatively similar, though some changes in the range of motion were observed. A reduction in shoulder elevation was measured during the SLING-assisted SFE and SAA tasks in the control group. This is to be attributed to the limited range of motion of the mechanism when elevating the arm. In the remaining tasks (H2M, RFUI, RFUC, PP) the SLING did not limit shoulder elevation, and the increments in shoulder elevation found in the control group were minimal but consistent in sign. These increments indicate that the SLING mechanism could have induced a small offset by pulling the arm upwards. In contrast to the control group, no reduction in shoulder elevation was found in the FSHD group when the SLING was used during the SFE and SAA tasks because of the already limited range of motion of this population. Despite the abovementioned offsets, the CMC values above 0.83 (in SAA, SFE, RFUI, RFUC and PP) indicate that the shoulder elevation angular waveforms with and without the SLING were similar in shape and offset, confirming the findings during reaching of Prange et al. and Coscia et al. [12, 13] for healthy persons. The angular waveforms of the H2M movements were less consistent, as indicated by a CMC value of 0.54, indicating an effect of the SLING on the kinematics. Concerning the way muscle activity is affected by the arm support, a general scaling of activity was found when using the arm support in both healthy and FSHD persons, as expected. This findings is in agreement with those of Prange, Coscia et al. in healthy and stroke persons. Concerning the way muscle activity is affected by the arm support, a general scaling of activity was found when using the arm support in both healthy and FSHD persons, as expected. The discussion on muscle onset that follows relates to the lifting phase of the reaching movements (from start to target). In this study it was hypothesized that performing tasks while using the SLING in FHSD persons would result in changes in individual muscle onset times. The findings appear to support this hypothesis only in some muscles. Additionally in the healthy control group some muscle onsets were also affected when using the SLING. The biceps' onset in the healthy group occurred later in both SLING-assisted reaching tasks, while the deltoid's onset was delayed only in the SLING RFUC task. However in the FSHD group, the onsets of biceps, deltoid were all delayed in both SLING-assisted reaching tasks with the trapezius being also delayed in the SLING-RFUC task. The biceps accomplishes the function of an arm forward flexor as well as elbow flexor, while the lateral deltoid serves as an arm abductor. As the activity of biceps and deltoid was relieved by the SLING, the later onset also appears to show that healthy controls and FSHD persons chose to

rely more on the inertia of the SLING to lift the arm, thus resulting in a later muscle involvement. In previous research of Bakhtiary et al. [7, 27], activation of the biceps has been found to be higher in persons with FSHD compared to healthy persons during tasks involving arm elevation. This behaviour is the result of an attempt by the biceps to compensate for the weakness of other arm elevators. Moreover, as pointed above, a later onset of the trapezius occurred in the FSHD group, but only in the SLING RFUC task. Contralateral reaching, compared to ipsilateral reaching, requires in principle more scapular mobility [28, 29] and dynamic scapular stability [30], both of which can be difficult to accomplish in people with FSHD [31]. The upper fibres of the trapezius provide scapular mobility through the upward rotation of the scapula [9], which increases with arm elevation [31]. A later onset, at a corresponding higher shoulder elevation angle, of the upper trapezius appears to show that the FSHD group relied more on the SLING to initiate the movement. The moment generated by the SLING on the humerus, that induces an abduction movement of the humerus, might have facilitated upward scapular rotation during the lifting phase, and could therefore have induced a later onset, as well as reducing the load and subsequent fatigue of the upper trapezius in the long term. In persons with FSHD the excessive activity of the trapezius has in fact been hypothesized as part of a compensatory strategy for the limited scapular rotation [7] and it is therefore relevant to consider how it is affected by the design of a specific support device. A common shift in onset activity however does not necessarily implies a different muscle control strategy. In this study in both healthy and FSHD groups no temporal shifts in activation onsets were observed between SLING and unsupported conditions in the deltoid-trapezius and deltoid-latissimus pairs, which appears to provide first-time evidence that the sequential activation of these muscles is unaffected by the arm support in persons with FSHD. The latissimus dorsi plays a role in balancing the abduction moment exerted by the counterweight, and thus it could be hypothesized that an earlier involvement of this muscle in the SLING condition would be required to resist the upwards pull of the mechanism. However the activation onset of the latissimus dorsi did not change relatively to the deltoid in persons with FSHD when using the SLING. It seems thus that both the FSHD and control groups were able to exploit the inertia of the mechanism to their advantage, without an earlier involvement of the latissimus dorsi. In addition, An abduction moment of the mechanism could also alter the force balance between the abduction moment of the deltoid and the abduction moment of the latissimus dorsi on the humerus [24], and thus eventually affect shoulder stability. However this hypothesis

remains unproved and should be the objective of future research where the synergies between the superficial shoulder muscle should also be taken into account [32].

Study limitations

Some methodological aspects can be listed as limitations of this study. The movement order was not randomized, with the unsupported condition always preceding the supported condition. Although this was done to prevent that the FSHD individuals would get too fatigued if the supported condition was done first and the unsupported (which required more effort) afterwards, future studies should include a randomization of conditions. The performance of MVC was carried out while one of the researchers provided resistance to the subject. This could have induced some variability in the way MVC was measured at baseline, since in some cases it was difficult to immobilize the joints properly by hand. In some movements, the maximum activity of the upper trapezius muscle as %MVC was higher than the EMG activity measured during MVC. It is possible that factors like reduced concentration or fear of contracting the muscles influenced the person's voluntary effort during MVC [33, 34]. Consequently this could have resulted in activation percentages above 100% of MVC during the execution of movements and tasks. Moreover, although the lower trapezius and serratus anterior muscles are both important scapular stabilizers, their activity were not recorded in this study. Finally, there was a 16 year mean age difference between the patient and control groups. While the FSHD individuals were free from orthopedic problems, there might have been structural changes in the shoulder affecting for example the articulation surfaces and tendons, as a result of the aging process.

Conclusions

The biomechanical changes induced by a counterweight arm support mechanism were described in a group of healthy controls and FSHD persons. An overall reduction in muscle activity was found, as expected, which confirmed previous research findings on healthy individuals. The SLING did not appear to significantly affect the shoulder elevation angle waveforms of healthy controls and FSHD participants, although SFE and SAA movements were hindered in healthy controls, resulting in lower elevation angles. However, using the SLING resulted in later activation onsets of biceps and

deltoid in both reaching tasks in the FSHD group. In addition, a later onset of the trapezius muscle characterized the use of the support device in FSHD participants during the reaching task to the contralateral side. This finding implies that the FSHD group was more inclined to use the inertia of the mechanism to their advantage when more scapular mobility was required, thus resulting in a later activation. These findings can lead to speculate that scapular function was aided in FSHD persons. However shoulder stability can also have been influenced by the introduction of external loads by the SLING. It is unclear whether these loads can affect shoulder articular structures or if they can be damaging with a long usage of the device. In future research, information on muscle activity should be complemented by that on joint moments and loads to characterize the profile of FHSD users of arm supports more accurately, while scapular stabilizers such as the lower trapezius and the serratus anterior should also be measured. This process should eventually lead to a personalized approach aimed at a customization of support devices in persons with FSHD.

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7

Different profiles of upper limb function in four types of neuromuscular disorders

Bergsma A., Janssen M. M., Geurts A. C., Cup E. H., de Groot I. J. Different profiles of upper limb function in four types of neuromuscular disorders. **submitted**

Abstract

Objective: The aim of this study was to explore upper extremity (UE) impairments, activity limitations and related participation restrictions in people with four different types of neuromuscular disease (NMD) - FacioScapuloHumeral Dystrophy (FSHD), Limb-Girdle Muscular Dystrophy (LGMD), Spinal Muscular Atrophy (SMA) and Duchenne Muscular Dystrophy (DMD) - and to investigate whether there are common profiles of UE function in these types of NMD.

Methods: Web-based administered questionnaires, including the Brooke classification and questionnaires covering UE impairments (pain and stiffness), activity limitations and participation restrictions were distributed amongst people with four types of NMD in the Netherlands. 267 respondents were included: FSHD (n=88), LGMD (n=65), SMA (n=64), and DMD (n=50).

Results: The reported problems by the FSHD and LGMD group were characterized by relatively high scores for pain and stiffness and low scores for activity limitations. Conversely, the experienced problems of the DMD and SMA group were characterized by relatively low scores for pain and stiffness and high scores for activity limitations.

Conclusions: Our results indicate specific profiles of UE function in different types of NMD. While the profile observed in persons with FSHD and LGMD seems to reflect overuse, the profile seen in persons with DMD and SMA is suspicious of disuse, each requiring a specific rehabilitation strategy.

7.1 Introduction

Existing treatments in neuromuscular disease (NMD) mainly focus on symptom relief. Rehabilitation, including physiotherapy, occupational therapy and speech therapy are widely used to increase or maintain the ability to participate in daily activities and society [1–3]. Particularly physiotherapy is widely applied for strength training, functional training, endurance training, and muscle stretching [1]. A Cochrane review on strength training and aerobic exercise training for muscle disease has shown that here are few high quality RCT's to show the efficacy of exercise training [4]. Recently our group was however able to show that aerobic exercise training can improve chronic fatigue and physical activity in people with FSHD [5] and that assisted bicycle training can delay functional deterioration in DMD [6]. In order to develop and test new treatment approaches in NMD, a thorough insight into the natural profile of each disease is necessary. Although the natural courses of the most common NMD have been described in the past [7], these descriptions were mostly focused on the level of muscle function and structure of the International Classification of Functioning, Disability and Health (ICF) [8], and hardly on the ICF-levels of activities or participation. In previous studies, we already investigated UE activity limitations in Duchenne Muscular Dystrophy (DMD) [9] and FacioScapuloHumeral Dystrophy (FSHD) [10] using a web-based questionnaire. The aim of this study was to document impairments (pain, stiffness), activity limitations and participation restrictions due to UE involvement also in people with Limb Girdle Muscular Dystrophy (LGMD) and Spinal muscular dystrophy (SMA) using the same self-report questionnaire that was used for people with FSHD and DMD, and to investigate whether common profiles of UE can be identified among these types of NMDs.

7.2 Methods

Participants and procedure

A web-based survey (QuestionPro; Survey Analytics LLC, Seattle, USA) was designed which covered the ICF-levels of structure and function, activities and participation. This survey included questions concerning arm pain and stiffness adapted from the University of Michigan Upper Extremity Questionnaire [11], the Brooke scale [12], the x (CUE) [13], the Abilhand questionnaire [14] with four added questions (here referred to as Abilhand-plus [9]) and open questions concerning participation [9]. In 2011, the survey was sent via the Dutch NMD patient organization 'Spierziekten Nederland' to their Dutch speaking members with DMD, FSHD, LGMD and SMA in the Netherlands (for DMD also via the Dutch Duchenne Parent Project). The results of the FSHD and DMD group were described separately before [9, 10]. In this study, the results of the LGMD and SMA group are described and compared to the results of the FSHD and DMD group (for persons with DMD only participants of the Netherlands, to make it comparable with the other groups, and avoid cultural differences). This procedure was approved by the medical ethical committee in the Arnhem-Nijmegen region (the Netherlands). The study has been performed in accordance with the ethical standards laid down in the Declaration of Helsinki.

Outcomes

Outcomes were divided into four categories (1) participant characteristics, (2) UE impairments, (3) UE activity limitations and (4) related participation restrictions.

Participant characteristics

The assessed participant characteristics were: age, time since diagnosis, hand preference, wheelchair confinement, and use of assistive devices for the UEs. For the analyses, the originally dominant arm was used in case hand preference had changed.

UE Impairments

The pain and stiffness scores were divided into the aspects frequency (range: 0-6, the higher the score, the higher the frequency), severity (range: 0-10, the higher the score, the more severe) and disablement due to pain or stiffness (range: 0-10; the higher the score, the more disabling). Combination scores were calculated for each segment of the dominant and non-dominant arm (shoulder, upper arm, elbow, lower arm, wrist, fingers, thumb) by taking the sum of the three aspects (range: 0-26). A similar approach was used before in the study by Janssen et al. [9]. Besides scores for each arm segment, total sum scores for both the dominant and non-dominant side of the UE were calculated (range: 0-182).

UE activity limitations

The Brooke scale was used to classify basic UE activities; the higher the score the more limitations [12]; the CUE was used to assess basic UE capacity [13]; and the ABILHAND-plus to assess the performance of daily activities [9, 14]. The CUE contains 32 items (30 items right/left arm, 2 items both arms) that can be scored on a 7-point scale (1 = unable to perform, 7 = can perform without difficulty). The CUE questionnaire in this study had 30 items in total, because the item “Hold a hammer” accidentally was missing for both the left and right arm. Four CUE dimensions (CUE lift/reach, CUE pull/push with arms, CUE arm/wrist moving and CUE hand/fingers use) were determined. These dimensions were based on the original validation of the CUE [13]. The ABILHAND-plus questionnaire contained 26 items (22 items that were described by Vandervelde et al. [14] and four additional items that were indicated as important by boys with DMD [9]) that were scored on a 3-point scale (0 = impossible, 1 = difficult, 2 = easy) or could be answered with “I don’t know”.

Participation restriction

Respondents were asked if they went to school, had a job, practiced sports, had hobbies, participated in household activities and were in a romantic relationship. Subsequently, for each of these social roles, participants were asked if they experienced restrictions due to UE impairments or activity limitations.

Statistical analysis

The mean, median and standard deviation were calculated for age, time since diagnosis, pain and stiffness combination scores, Brooke scale and the four CUE dimensions. The proportional scores of the CUE dimensions were calculated by dividing the sum of the associated items by the maximum possible score of these items. The percentage of respondents was calculated that: 1) experienced pain or stiffness in a certain UE segment (combination score > 1) on either the right or left side; 2) answered a CUE activity to be very, extremely or totally limited; and 3) answered an ABILHAND-plus activity to be difficult or impossible. When the participants did not fully complete the questionnaire, all available items were included in the analysis. To compare the percentages of pain and stiffness complaints between the four groups, Wilcoxon rank-sum tests were used. Bonferroni correction was applied to compensate for post-hoc testing. To compare the CUE dimensions between the four groups, Kruskal-Wallis tests were used. All statistical analyses were done using IBM SPSS Statistics version 22 for windows (IBM®, Somers, USA).

7.3 Results

In total 267 respondents were included in this study (FSHD=88, LGMD=65, SMA=64, DMD=50), of which 222 completed the whole survey (including the questions on participation). The mean age in de DMD group was 15 years, whereas in the SMA, LGMD and FSHD group the mean age varied from 39 to 51 years. In the FSHD and LGMD group, less than 23% of the respondents was wheelchair confined, whereas more than 64% of the respondents was wheelchair confined in the SMA and DMD group. The use of arm supports was highest in the SMA group (28.1%) and lowest in the LGMD group (11.5%). When considering Brooke scores of 2 to 6, representing people that could benefit from arm supports, respectively 19.4, 20.3, 36.7 and 27.8 percent of the persons with FSHD, LGMD, SMA and DMD reported use of such a device. The mean Brooke score was highest in the DMD group and lowest in the LGMD group. The patient characteristics are presented in Table 1.

Table 1: Tasks that were executed by the participants

	FSHD	LGMD	SMA	DMD
N	88	65	64	50
N completed survey	71	49	55	47
Mean age (yrs)	51.1	46.2	39.1	15.2
Mean time since diagnosis (yrs)	19.1	11.7	25.4	10.8
Preferred hand (% right)	81.0	89.0	84.4	84.0
Wheelchair confined (%)	17.6	23.0	71.9	64.0
Use arm support (%)				
In total	17.6	11.5	28.1	18.0
Brooke score 2-6	19.4	20.3	36.7	27.8
Brooke score (mean)	2.8±1.0	2.3±1.3	2.9±1.4	3.1±1.9

UE impairments

Pain in the shoulder and upper arm was more often reported in FSHD than in LGMD, SMA or DMD (all $p<0.05$). Pain in the lower arm and thumb was reported more often in FSHD than in LGMD (lower arm: $p=0.03$ and thumb: $p=0.05$) (Figure 1). Persons with FSHD not only reported pain most frequently, they also reported the highest pain combination scores in the shoulders compared to persons with LGMD, SMA and DMD ($p=0.05$, $p<0.01$ and $p<0.01$, respectively). The upper arm, wrist, thumb and finger pain scores reported by persons with FSHD were significant higher compared to the scores reported by persons with DMD ($p<0.01$, $p=0.02$, $p=0.02$ and $p=0.05$, respectively). Finally, the pain score of the upper arm reported by persons with FSHD was higher compared to the scores reported by persons with SMA ($p<0.01$) (Figure 2).

Stiffness in the shoulders was reported most often by respondents with FSHD and LGMD (66% and 69%, respectively). Stiffness in the shoulders was reported significantly more often by persons with FSHD and LGMD compared to persons with DMD ($p=0.04$ and $p=0.03$, respectively). Differences in the percentages of participants reporting stiffness complaints in other parts of the arm were present, but not significant (Figure 1). The highest stiffness combination scores were reported by persons with FSHD and LGMD in the shoulders and upper arms (Figure 2). The stiffness score of the shoulders reported by respondents with FSHD was significantly higher than the score reported by respondents with DMD ($p<0.01$) and the upper arm score was significantly

higher in the FSHD group compared to the SMA and DMD group (p=0.02 and p=0.02, respectively). Between the FSHD and LGMD group, no significant differences were found between the stiffness scores (p>0.05).

UE activity limitations

Items of the CUE that required reaching and lifting were limited in all four types of NMD. Respondents with SMA and DMD reported in general more activity limitations in all CUE dimensions than persons with FSHD and LGMD, whereas no significant differences were found between FSHD and LGMD nor between SMA and DMD (p>0.05) (Figure 3 and Figure 4).

Most UE activity limitations were reported by persons with DMD and SMA, who reported 37 and 24% of the ABILHAND-plus activities being impossible to perform and 32 and 26% difficult to perform, respectively. In FSHD and LGMD, 2 and 5% reported that activities were impossible and 26 and 17% that activities were difficult to perform, respectively. On average, 72% of the participants with FSHD reported activities to be easy to perform and in LGMD this was 78%. In SMA and DMD, this was 44 and 37%, respectively (Figure 4).

Participation restrictions

Of the respondents with DMD, 73% went to school and 71% experienced UE-related restrictions at school. For the respondents with FSHD, LGMD and SMA, the corresponding percentages were 11% / 50%, 14% / 71% and 14% / 88%, respectively. About half of the respondents with FSHD (51%), LGMD (49%) and SMA (55%) participated in work versus 21% for DMD. More than 60% of all groups experienced UE-related restrictions at work. Participation in sports varied from 30% in the FSHD, LGMD and SMA groups to 47% in the DMD group. At least 86% in all groups experienced UE-related restrictions in sports. The majority of the respondents (DMD 85%, LGMD and SMA 90%, and FSHD 94%) participated in hobbies. More than 70% (DMD and SMA) or 80% (FSHD and LGMD) experienced UE-related restrictions in this domain. If respondents participated in household activities (75% in FSHD and LGMD; and 42% in SMA. This question was not asked to people with DMD), UE-related restrictions were

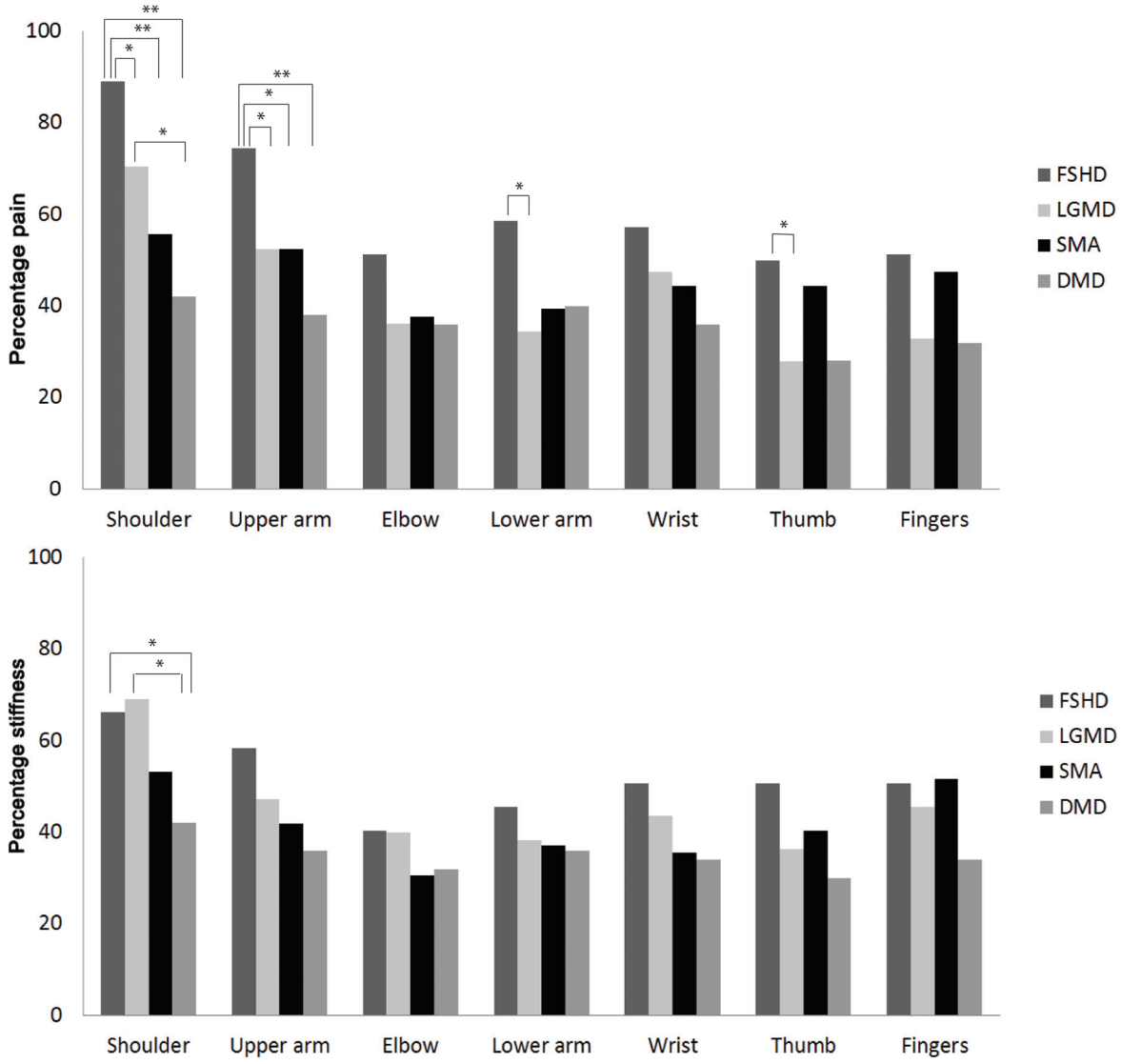

Figure 1: Percentage of participants mentioning having pain (top) and stiffness (bottom). (Pain and stiffness scores > 1, *: $p<0.05$, **: $p<0.01$)

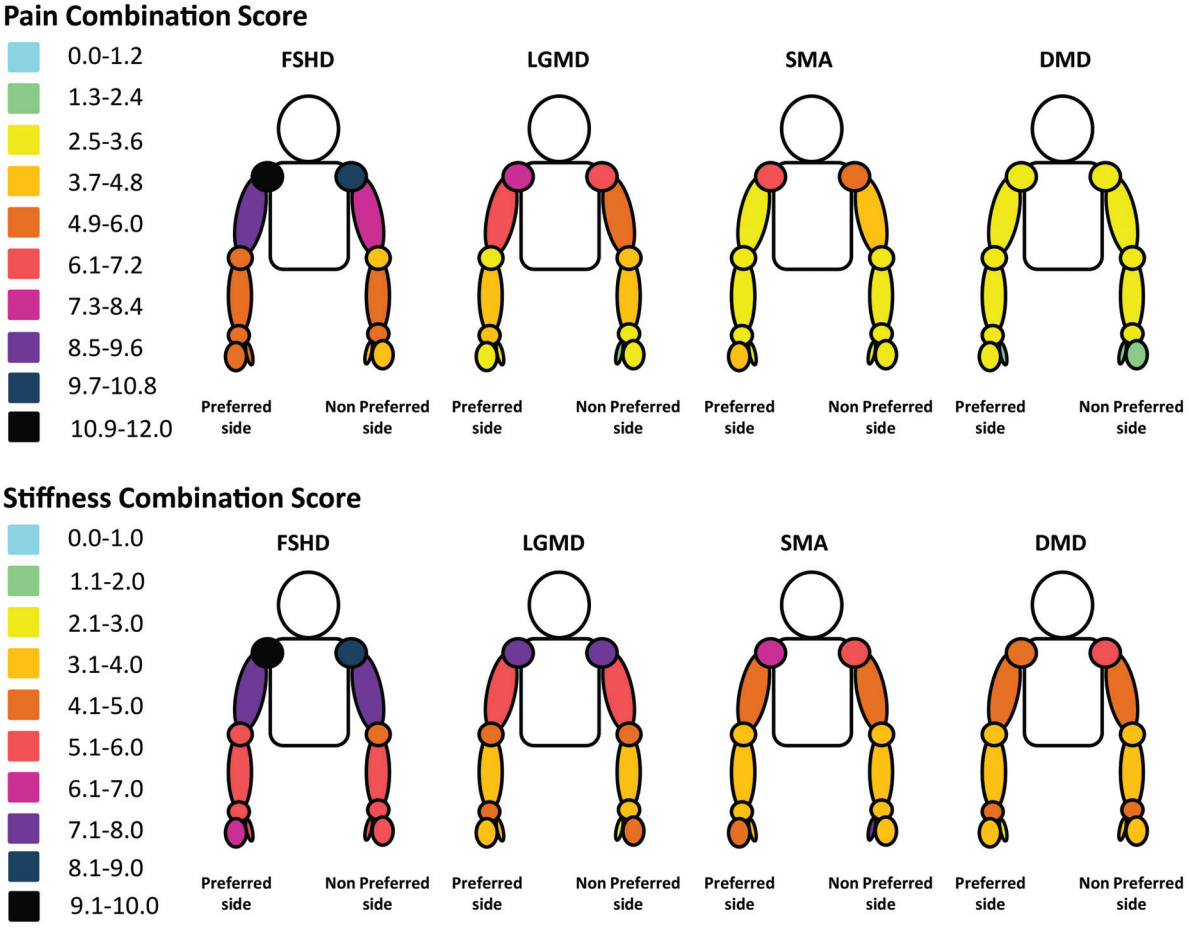

Figure 2: Average pain and stiffness combination scores for the different NMD per body segment (maximal possible pain and stiffness score = 26)

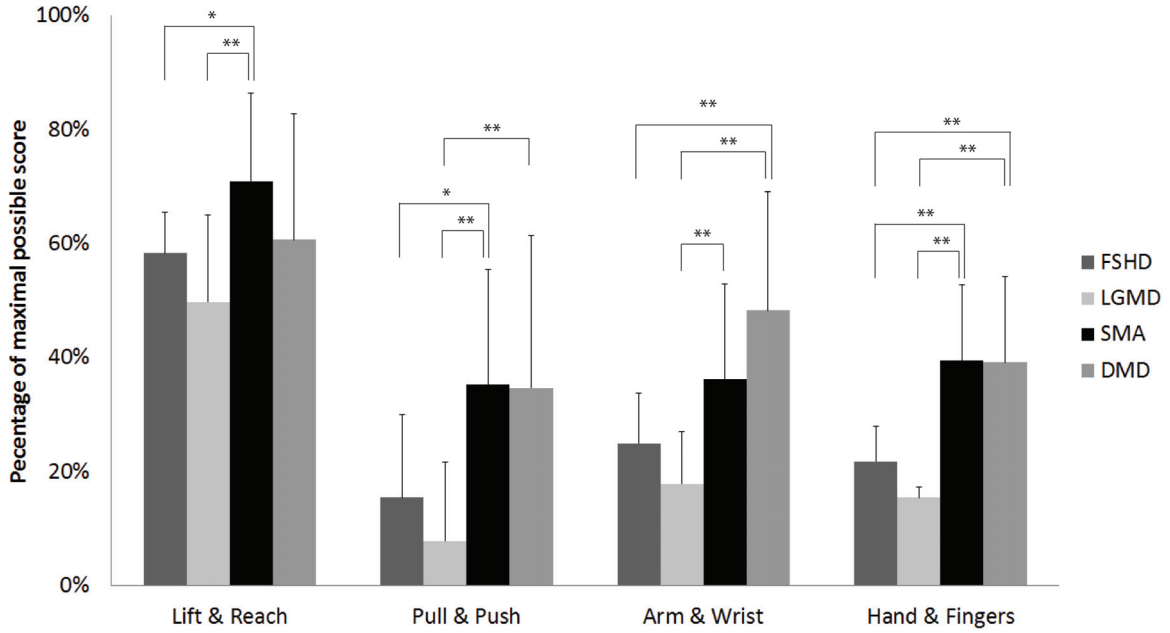

Figure 3: Capacity of Upper Extremity. Data points represent mean CUE scores as percentage of the maximal possible score, with standard deviations. The higher the percentage, the more difficulties were experienced. (**: $p<0.01$; *: $p<0.05$)

reported by 78% of the SMA group, 89% of the LGMD group and 93% of the FSHD group. More than 80% of the respondents with FSHD and LGMD were involved in a romantic relationship, compared to 51% of the SMA group and 0% of the DMD group. Of those with a romantic relation, 71% reported that they experienced UE-related restrictions in maintaining this relationship.

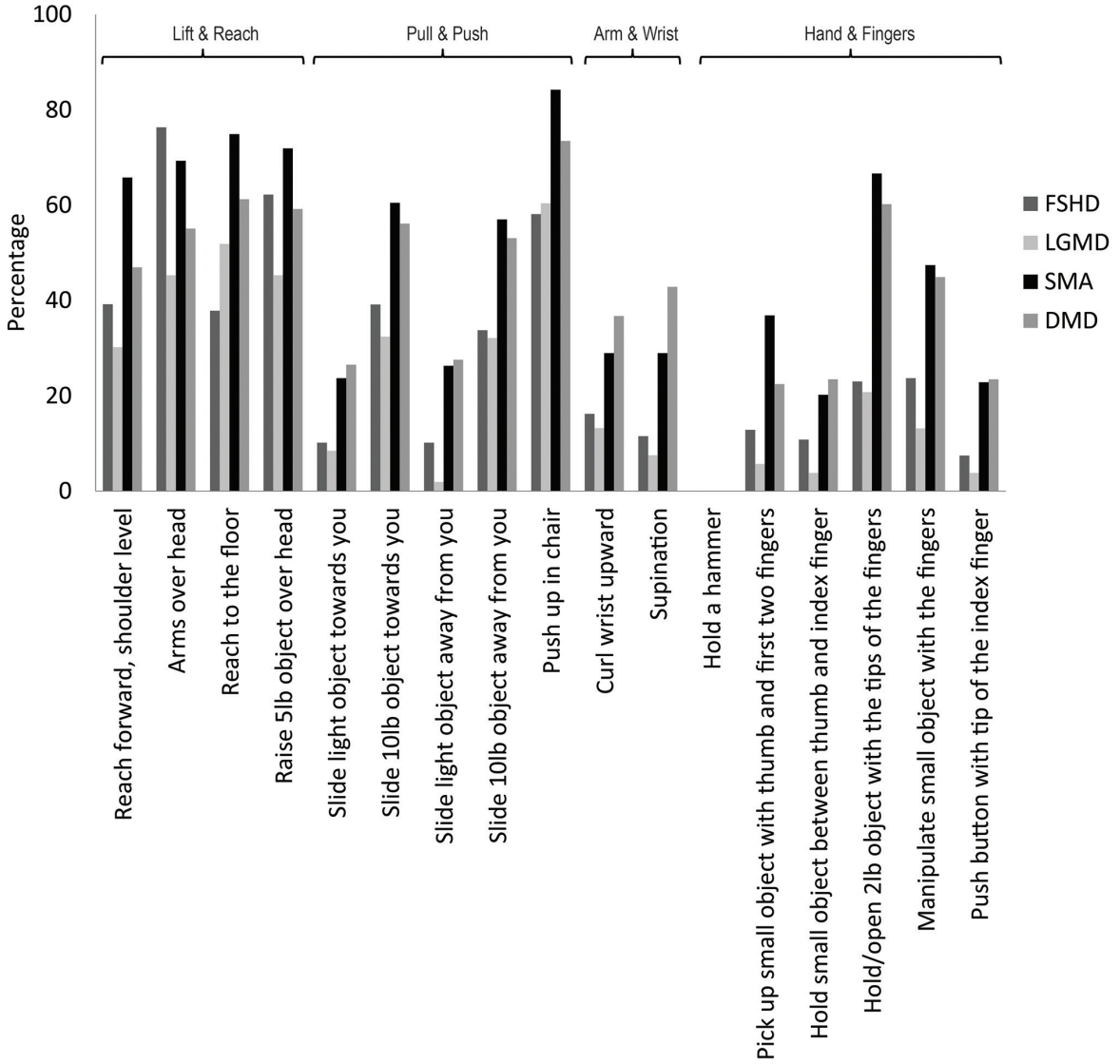

Figure 4: Individual Percentage of participants that mentioned being very, extremely or totally limited in performing certain CUE activities (item "holding a hammer" is missing).

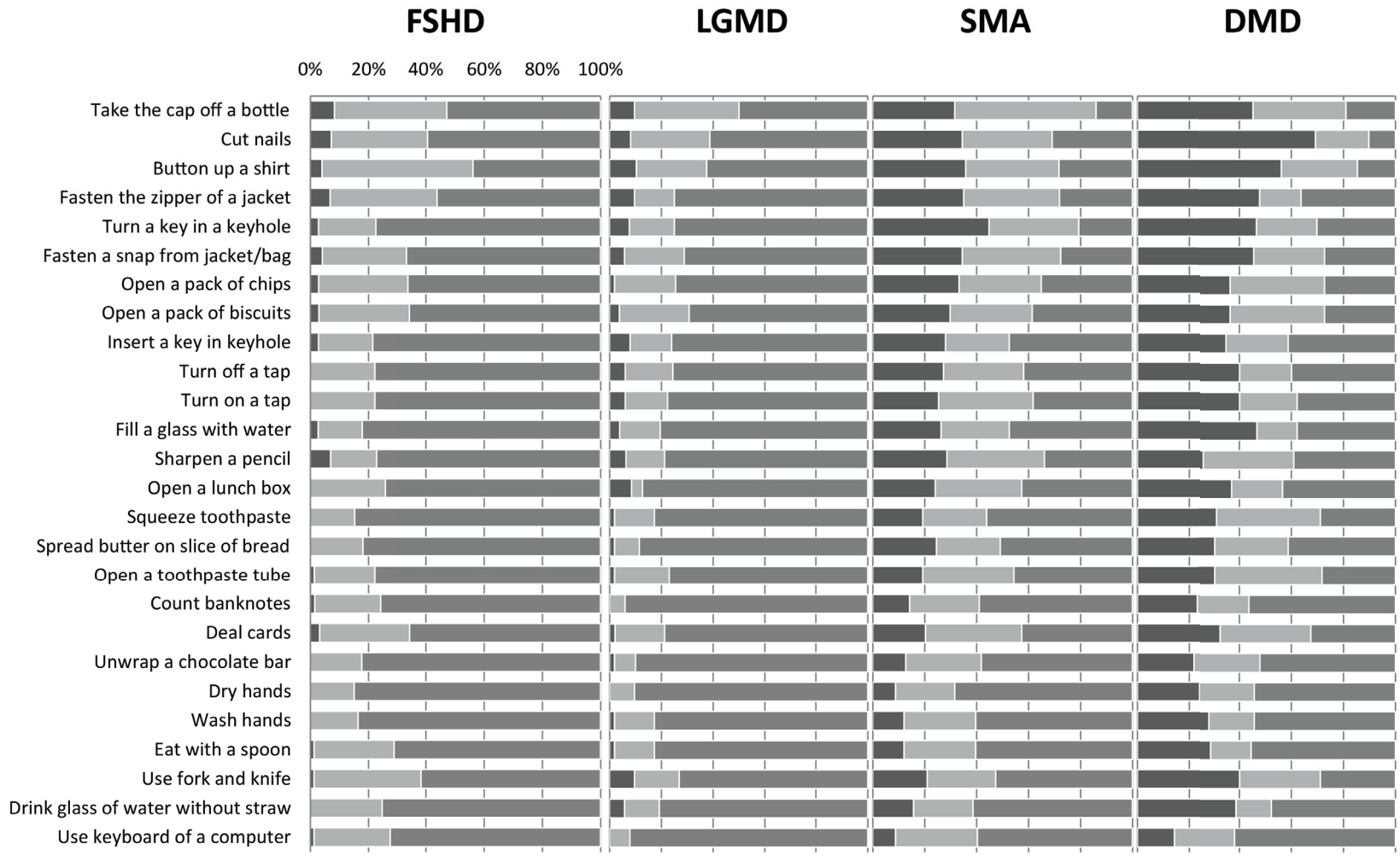

Figure 5: Difficulty in performing ABILHAND-plus scores. Percentage of participants that mentioned certain ABILHAND-plus activities being impossible (black), difficult (light grey), or easy (dark grey)

7.4 Discussion

The aim of this research was to study impairments (pain, stiffness), activity limitations and participation restrictions due to UE involvement in people with FSHD, LGMD, SMA and DMD using self-report measures and to investigate whether common or different profiles could be identified. About 20 years ago, a series of profiles was published concerning FSHD, LGMD, SMA and DMD [15–18] that described the general changes in muscle strength and provided a good understanding of the experienced impairments in these patient groups. The perspective of the current study aimed not only at UE impairments, but also at activity limitations and participation restrictions due to UE involvement using uniform self-reported outcome measures. We found a large impact of UE impairments on daily activities and societal participation in persons with NMD, emphasizing the importance of rehabilitation interventions aimed at reducing or compensating for the activity limitations and participation restrictions related to UE impairments.

We previously reported UE impairments and activity limitations separately for people with FSHD and DMD [9, 10]. In current study these populations were compared with each other as well as with people with LGMD and SMA to investigate whether common or different profiles could be identified among the different types of NMD. In general, the profile of UE activity limitations in SMA was quite similar to that observed in DMD, while the profile of UE activity limitations in LGMD showed similarity to that of FSHD, however, major differences were observed between LGMD and FSHD on the one hand and SMA and DMD on the other hand. Based, on the ABILHAND-plus, limitations in UE activities were less often reported by persons with FSHD and LGMD than by persons with SMA and DMD.

Pain was reported by more than 30% of the respondents in one or more segments of the UE, and the highest frequencies of pain were reported by people with FSHD in the shoulder and upper arm. Also in previous studies, it has been shown that pain is reported frequently in persons with different types of NMD, including FSHD, LGMD, SMA and DMD (frequencies ranging from 54%-96%) [19–22]. In this study, we found a similar profile for stiffness as for pain. Pain and stiffness are not always easily discerned from each other as subjective feelings. This could be explained by

the relation between pain and stiffness (correlation coefficients ranging from 0.44 to 0.83 and $p<0.01$).

Looking at functional limitations measured with the Abilhand-plus, we found that despite the high pain and stiffness scores in persons with FSHD and LGMD, the limitations in activities were less prominent than in persons with SMA and DMD. An explanation for this finding may be that people with FSHD and LGMD are inclined to overuse their UE, whereas in people with SMA and DMD there is a decrease in use of the UE due to higher muscle weakness in the disease course.

The above-mentioned notion can give direction to differential rehabilitation strategies. Pain is an important complaint in both FSHD and LGMD and often remains unaddressed and untreated in the NMD population [19]. If pain is a sign of overuse in FSHD and LGMD, education to avoid dysfunctional compensation strategies should be a key strategy in addition to exercises to improve muscular coordination during functional movement with or without the use of arm supports. Due to lack of strength there is a higher risk of inactivity and minimal use of the arms in DMD and SMA. This results potentially in less pain, but also in decreased use of the upper limb, which in itself may result in further loss of UE function [6]. New insights have shown that UE training in DMD is likely to result in the retaining of improved UE function. A recent study showed that young men with DMD retained significantly more UE function six months after assisted UE training compared to a control group of DMD patients without such training [6, 23]. In the current study it was remarkable that, despite the high percentages of severe UE limitations, less than 50% of the persons that could possibly benefit from an arm supportive device reported the use of such a device. In a review on the effectiveness of dynamic arm supports, there was already concluded that the use of such supports in the home situation is often very low [24]. Our results show that there are different profiles of UE function in people with NMD that call for a personalized approach instead of a one-size-fits-all solution.

Study limitations

The questionnaire that we used was originally designed for people with DMD. Since DMD is extremely rare in women, gender was not asked for in this study. The questionnaire we used was self-reported and, therefore, represented the patients' perspectives.

Thus, the pain and stiffness scores did not provide insight in the actual impairments of muscles and/or joints causing the pain and stiffness complaints. Some of the items of ABILHAND-plus questionnaire addressed activities typical of adulthood, such as cutting nails. These items may have been hard to answer by the younger adolescent respondents.

Conclusion

This study provides a unique overview of UE function in people with various types of NMD based on self-reported outcomes. It shows that pain and stiffness are highly prevalent impairments and that many people experience activity limitations and participation restrictions due to UE involvement. While persons with FSHD and LGMD experienced relatively severe pain and relatively few activity limitations, persons with DMD and SMA showed the opposite pattern. These distinct profiles may be related to predominant ‘overuse’ (FSHD and LGMD) and ‘disuse’ (DMD and SMA), respectively, and provide clues as to what rehabilitation strategy would be most appropriate from a personalized healthcare perspective.

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8

Summary and general discussion

8.1 Summary

Upper limb movements play a fundamental role in the performance of daily life activities. There are various neuromuscular disorders (NMD) that can impair the ability to use the upper limbs properly, which may influence people's quality of life. Typical conditions that have an impact on the ability to use the upper limbs are Facioscapulohumeral Dystrophy (FSHD), Limb-girdle Muscular Dystrophy (LGMD), Duchenne Muscular Dystrophy (DMD) and Spinal Muscular Atrophy (SMA). To improve the quality of life of people living with NMD who experience severe upper limb impairments, it is important to facilitate the performance of activities of daily living (ADL). This can, for example, be achieved by using assistive devices that augment arm function.

The aim of this thesis was to study upper limb function in people with FSHD and to compare this function between FSHD and other types of NMD that are known to affect the upper limbs. Several approaches were used: first, a literature review was performed, followed by a survey to explore the influence of upper limb activity limitations in FSHD on daily life. These results were compared to other NMD with known upper limb involvement (LGMD, SMA, and DMD) by means of the same questionnaires. Finally, laboratory studies were conducted to examine the arm in a 3D-environment combined with muscle activation patterns with and without arm support.

Upper limb assistive technology for people with DMD

Chapter 2 describes the outcomes of a workshop about the requirements for upper limb function research and the state-of-the-art assistive devices that can be used to support upper limb function. This workshop focused specifically on DMD, because in this group upper limb function and the use of supportive devices have been investigated before. The primary goal of the workshop was to bring people from different disciplines together and discuss opportunities to accelerate the development of upper limb assistive technology for enhancing the functional abilities of non- ambulant men with DMD. Twenty-four participants representing parents, experts in user requirements,

human-machine research, electrical and mechanical engineering, and clinicians involved in the care of children with DMD from Denmark, the Netherlands, the UK and the USA participated in the workshop. The workshop addressed the user requirements, the current methods for the evaluation of arm function, the commercially available arm supports, the current research projects towards active arm supports, and emerging technologies that could be useful for the future development of assistive technology for people with DMD. In order to improve quality of life for those living with Duchenne, independence and participation must be facilitated. It was stated that individuals with DMD express an urgent need for privacy, for example during toilet use. Social contacts and employment are indicated as priorities as well. Current available arm support devices are still not widespread used at home. There are several initiatives that aim to develop solutions that better suit the needs of (young) men with DMD. In order to optimize devices and assess effectiveness of devices, quantitative and objective evaluation methods are needed as well as clinical validation methods to assess the value of these new prototypes under operating conditions. Quantitative data comprise kinematic parameters, such as the range of motion of supported arm movements, and the muscle effort that is needed for using a particular type of arm support. To assess upper limb function, among other things, evaluation of reachable workspace was mentioned. This construct has demonstrated its applicability as a marker of upper limb function in DMD. Besides the assessment of upper limb functions, there is a need for outcome measures to evaluate how much the upper limbs are used during the day. Six clusters of actions were identified. These were: (a) identifying user and caregiver needs and acceptance, (b) assess performance of user and caregiver before and after fitting a device, (c) develop lab and mobile testing metrics and protocols, (d) gather data on use of devices, (e) develop modular technology, and (f) work on accessibility and reimbursement in different countries.

Review on upper limb function and activity in FSHD and LGMD

Chapter 3 comprises a literature review of what is known about the natural course of upper limb functions and capacities in persons with FSHD and LGMD. Both FSHD and LGMD are slowly progressive diseases that have a typical age of onset between 10 and 30 years of age. This study also gives an overview of outcome measures that are used to evaluate upper limb function and activities in patients with FSHD and LGMD.

A search of the PubMed, MEDLINE, EMBASE, CINAHL and Cochrane databases was performed using the MeSH terms and free text words “fshd” OR “facioscapulohumeral” OR “limb girdle muscular dystrophy” in combination with “upper extremity” OR “arm” OR “hand”. This search yielded in 247 articles, and the final selection included 16 articles. The included studies comprised a total of 272 patients with FSHD (mean age ranging from 36 to 59) and 270 patients with LGMD (mean age ranging from 35 to 55). It was concluded that the clinical picture of upper limb impairments and activity limitations in FSHD and LGMD patients is highly variable. In general, FSHD and LGMD patients experience difficulties while elevating their arms. The execution of tasks takes a considerably longer time. The clinical course of upper limb functions and capacities in persons with FSHD and LGMD is hard to predict due to a high variability. To evaluate upper limb function in FSHD and LGMD patients, manual muscle testing (MMT) is the most commonly used method. In this review, it was not possible to compare MMT results between various studies, as most of the studies reported a composite score of strength instead of scores for the various muscle groups. Although MMT is considered to be a valid measure to determine disease progression, MMT is a rather unreliable method for assessing isometric muscle strength. One study used electromyography (EMG) recordings of several muscles (biceps brachii, brachioradialis, triceps and deltoid anterior) during a simulated drinking task. The researchers found that EMG activity during this task was higher in a FSHD group than in healthy controls. The muscle activity and movement patterns in the FSHD group included more synergistic muscle activity and more abduction and flexion of the shoulder and elbow joints. To evaluate people’s capacity to use the arms during activities, the Brooke scale (scores ranging from 1 to 6) is mostly used. Relatively few people with FSHD reported, however, a Brooke score of 5 or 6, making the Brooke scale not sensitive to measure small differences in upper limb capacity. Besides, the Brooke scale only classifies the capacity of basic reaching activities of the arm and hand. More specific measures to evaluate upper limb capacity and performance during daily activities have not been used. Although measures like MMT and the Brooke Scale are often used, this review showed that there is a lack of more specific outcome measures to assess upper limb function, capacity and performance. It was stated that measures such as 3D motion analysis and EMG recordings are needed to provide additional insight in upper limb function. Moreover, questionnaires like the Abilhand are recommended to assess upper limb capacity, whereas accelerometry is recommended to assess upper performance in daily life.

Upper limb function and activity in FSHD

In **chapter 4**, the upper limb in people with FSHD was studied by using questionnaires at the level of impairments, activity limitations and participation restrictions. A web-based survey was designed, which covered these dimensions of the International Classification of Functioning Disability and Health of the World Health Organization (ICF). On the dimension of upper limb function, the survey included questions concerning pain and stiffness adapted from the University of Michigan Upper Extremity Questionnaire. To assess the capacity of using the arms during basic activities, the Brooke scale and the Capabilities of Upper Extremity Questionnaire (CUE) were used. The Abilhand-plus questionnaire was included to assess the capacity during daily activities. Moreover, open questions concerning participation were included. Eighty-eight persons with FSHD answered the questions. Besides the well-known problem of lifting the arms above shoulder level in FSHD, upper limb activities below shoulder level during vocational and occupational activities also appeared to be problematic in patients with FSHD. More than 40% of the respondents with FSHD experienced pain in one or both arms. The results showed that increased pain and stiffness scores and longer disease duration were associated with increased activity limitation. About 80% of the respondents indicated restrictions at work and while participating in sports, hobbies, household activities and romantic relationships.

Upper limb kinematics and muscle activation patterns in people with FSHD

Persons with FSHD have an increased risk of tendon or muscle damage due to compensatory movements that are often used to lift the upper limb and to over- come the lack of strength of the scapula-stabilizing muscles. Innovative arm supports may help persons with FSHD to perform arm activities that would cost considerable effort or might cause possible damage. In order to optimize devices and assess their effectiveness, quantitative and objective evaluation methods are needed. Quantitative data comprise kinematic parameters, such as the range of motion of arm movements and muscle effort that is needed to move the arms. A study of Bakhtiary et al. provided the first knowledge of arm function in FSHD during a simulated drinking task. However, muscles that are responsible for stabilizing the scapula were not investigated. In **chap-**

ter 5, the kinematics of the upper limb and the involvement of specific proximal muscles (biceps brachii, deltoid (lateral part), triceps brachii, trapezius (upper part), pectoralis major (clavicular part) and latissimus dorsi) during singular joint movements, reaching tasks and gross motor tasks were studied in persons with FSHD and healthy controls. Eleven persons with FSHD and eight healthy volunteers participated. Participants were asked to perform a set of six standardized movements (shoulder abduction-adduction, shoulder flexion-extension, reaching to the ipsilateral and con- tralateral side at shoulder level, moving the hand to the mouth and pulling-pushing of an object on a table). For each person and each task, the mean of the maximum upper limb elevation and minimum and maximum elbow flexion angle was calculated. All persons were able to complete the two reaching tasks and the two gross motor tasks. We found kinematic differences between the FSHD group and a healthy control group, mainly in the shoulder elevation angle during single shoulder movements and both reaching tasks. Only one person with FSHD was able to elevate the arm above 120º during the shoulder abduction-adduction and flexion-extension movements. Compared with healthy subjects, persons with FSHD activated their shoulder muscles to a greater extent during movements that required arm elevation. The median activity of the trapezius during the single shoulder movements was close to the muscle activity during maximum voluntary contractions. Moreover, deltoid and pectoralis muscles were highly active. It was concluded that higher activation of the trapezius in subjects with FSHD indicates a mechanism that could help to support impaired shoulder muscles during arm elevation at shoulder height. Visual inspection of the timing of muscle activations did not show any difference between the control group and the FSHD group.

Effect of forearm gravity compensation on upper limb kinematics and muscle activation in persons with FSHD

Arm supports are developed to compensate for loss of arm function. In **chapter 6**, the effect of forearm gravity compensation on kinematics and muscle activity of participants with FSHD and healthy participants was studied during the performance of standardized upper extremity tasks (shoulder abduction-adduction, shoulder flexion- extension, reaching to the ipsilateral and contralateral side at shoulder level, moving the hand to the mouth and pulling-pushing of an object on a table). Eleven persons with FSHD (Brooke scores 2 to 3) and eight healthy controls were instructed to perform the set of

movements, first with and subsequently without the aid of a SLING forearm support mechanism. Changes in shoulder kinematics and muscle activity were quantified while participants performed a set of standardized tasks with and without the SLING support mechanism. Shoulder abduction and flexion movements were hindered in healthy controls, resulting in lower elevation angles. These movements were not hindered in the persons with FSHD. Execution times were shorter during the SLING- assisted shoulder and hand to mouth movements compared to the none supported tasks, but longer in the SLING-assisted reaching and pull/push tasks. Movement of the trunk decreased when the SLING was used during the shoulder flexion extension movement, in both the control and the FSHD group. As expected, an overall reduction in muscle activity was found when the SLING was used, which confirmed previous research findings in healthy individuals. Using the SLING resulted in later activation onsets of biceps and deltoid during both reaching tasks in the FSHD group. In addition, a later onset of the trapezius muscle was found during the contralateral reaching task in the FSHD group. This finding implies that the FSHD group used inertial mechanisms more to their advantage when more scapular mobility was required, resulting in a later activation of the trapezius muscle. To characterize the profile of arm support users more accurately, information about muscle activity should be complemented by information about joint moments and forces, while scapular stabilizers such as the lower trapezius and the serratus anterior should also be measured.

Different profiles of upper limb function in four types of NMD

The web-based survey that was sent to the FSHD group (chapter 4) was also sent to a group of people with DMD, LGMD, and SMA. In **chapter 7**, the impairments, activity limitations and participation restrictions related to the upper extremity that were reported by people with FSHD were compared to those reported by people with LGMD, SMA and DMD in the Netherlands. The aim of this study was to investigate whether different profiles of upper limb function can be identified among these types of NMDs. On the level of upper limb function, the web-based survey included questions concerning pain and stiffness. To assess the capacity of using the arms during basic activities, the Brooke scale and the Capabilities of Upper Extremity Questionnaire (CUE) were used. The Abilhand-plus questionnaire was included to assess the capacity during daily activities. Moreover, open questions concerning participation were included. In

total 267 respondents were included (FSHD=88, LGMD=65, SMA=64, DMD=50), of which 222 completed the whole survey. The mean age of de DMD group was 15 years, whereas in the SMA, LGMD and FSHD groups the mean age varied from 39 to 51 years. In the FSHD and LGMD groups, less than 23% of the respondents was wheelchair confined, whereas more than 64% of the respondents was wheelchair confined in the SMA and DMD groups. The use of arm supports was highest in the SMA group (28.1%) and lowest in the LGMD group (11.5%). When the people that could benefit from arm supports were selected (Brooke scores 2 to 6), use of arm support was reported by 19.4%, 20.3%, 36.7% and 27.8% of the persons with FSHD, LGMD, SMA and DMD, repectively. The mean Brooke score was highest in the DMD group and lowest in the LGMD group. Pain in one or more segments of the upper limb was reported by more than 30% of the respondents. The highest frequencies of pain were reported by people with FSHD in the shoulder and upper arm. The reported pain scores related strongly to the reported stiffness scores, and it was suggested that pain and stiffness may not always easily be discerned from each other as subjective feelings. Most upper limb activity limitations were reported by persons with DMD and SMA, who reported 37 and 24% of the ABILHAND-plus activities being impossible to perform and 32 and 26% difficult to perform, respectively. In FSHD and LGMD, only 2 and 5% reported that activities were impossible and 26 and 17% that activities were difficult to perform, respectively. Similar to the FSHD group, the reported problems by persons with LGMD were characterized by relatively high scores for pain and stiffness and low scores for activity limitations. In contrast, the profile of the DMD and SMA group was characterized by relatively low scores for pain and stiffness and high scores for activity limitations. These results indicate distinct profiles of upper limb function in different types of NMD. While the profile observed in persons with FSHD and LGMD seems to reflect overuse, the pattern seen in individuals with DMD and SMA is more suspicious of decreased use of the upper limb. It is suggested that each pattern requires a particular rehabilitation strategy.

8.2 General discussion

Arm and hand movements are essential for proper functioning in everyday life. In neuromuscular disorders like Facioscapulohumeral Dystrophy (FSHD) the ability to use the arms and hands is often impaired, which may influence people's social participation and quality of life. Impaired upper limb function during activities of daily living (ADL) can be supported by technological interventions like dynamic arm supports. Dynamic arm supports are devices that assist the human arm during movement against gravity. There are various types of dynamic arm supports available [1, 2] that can be categorized into non-powered and powered devices [3, 4]. Depending on user requirements, these devices may support according to the principle of assist-as-needed or by completely lifting the arm [5]. While the effectiveness of dynamic arm supports has been demonstrated under laboratory conditions, the actual use of these devices at home is often low [1]. The main focus of this thesis was to study arm functioning of FSHD patients and, subsequently, to evaluate the effect of dynamic arm support on arm functioning. This thesis was part of the McArm project that intended to develop a new type of arm support that is motion controlled for which insight in the contributing factors to arm movement is needed.

The following discussion consists of two parts. First, the studies that are conducted in this thesis are discussed within the context of recent studies done by others. In the second part, remaining gaps are identified and recommendations are made to fill these gaps. To classify functioning and to structure the measures that were used in this thesis and those that are recommended for future research, the classification of the International Classification of Functioning, Disability and Health (ICF) was used (Figure 4). The ICF was developed by the WHO and provides a framework for classifying health and disability at both the individual and population levels [6].

Body functions and structures

In this thesis we studied 3D arm movements in relation to standardized EMG, which is based on the EMG during maximum voluntary contractions as these are used during manual muscle testing (MMT). MMT is considered as a valid measure to determine disease progression. It is, however, also argued that MMT is a rather unreliable

method for assessing isometric muscle strength. This could have influenced the standardized EMG outcomes. To determine the mobility of the human arm, passive range of joint motion (ROM) in the sagittal, horizontal and frontal planes, a standard method in physiotherapy [7], is often used. In this thesis, we measured active ROM in the shoulder and elbow joints during a set of single joint movements in a laboratory setting, combined with electromyography (EMG) of several shoulder muscles. This was also done by Bakhtiary et al. [8] for one task. The results were well comparable. We asked participants to execute the activities first without and subsequently while using a SLING arm supportive device. This provided insight in the ROM at the shoulder and elbow joints. These investigations helped to understand the added value of arm support at the level of muscles activity and range of joint motion for people with FSHD. We also looked at changes in muscle activity and shoulder ROM when using a SLING dynamic arm support. From these studies, we learned that the utilization of a forearm support mechanism by people with FSHD can increase the shoulder ROM, and reduce muscle activity. The finding that forearm support reduces muscle activity in people with NMD is in line with what other studies have shown. Kooren et al. [9] showed for example that upward and forward movements were experienced easier to perform by persons with DMD when they used dynamic arm support. Beside the quantitative objective measures, we were also interested in subjective impairments that people report. We asked people about pain and stiffness in the different parts of the upper limbs. We found that people with FSHD and LGMD reported relatively higher scores for pain and stiffness compared to people with DMD and SMA. Pain was also mentioned by others as a common problem among patients with NMDs [10, 11]. The difference between various NMDs has however not been studied before.

Activity and participation

In the activity and participation domains, two qualifiers are provided by the World Health Organisation [6], namely capacity and performance. Capacity describes an individual's ability to execute a task or an action, and indicates the highest probable level of functioning of a person in a given domain at a given moment. Performance describes what an individual does in his or her current environment. To classify capacity limitations in FSHD and LGMD, the Brooke scale is most often used (see review, chapter 3). The Brooke scale is, however, not sensitive enough to measure small differences in upper limb capacity. Besides, the Brooke scale only classifies the capacity of basic reaching

activities of the upper limb. Therefore, the studies of this thesis included the CUE and Abilhand questionnaires. These questionnaires were useful to explore at a group level during which activities people face most limitations. With these measures, we were able to identify two different capacity patterns (overuse and under-use) between different types of NMD. These profiles have not been described by others before. Based on these profiles, more group and individual treatment approaches could be developed. For example in FSHD and LGMD, it could help to make patients more aware of possible overuse and negative compensatory strategies. Positive compensation strategies can be stimulated next to using devices and finding a balance between physical activity and resting periods. In SMA and DMD, people can be enabled to move by means of devices to maintain joint mobility and muscle length.

Recommendations

Active ROM at the shoulder and elbow are calculated from the 3D motion capture data that was recorded in the motion laboratory. Although active ROM in the shoulder and elbow tells us something about overall arm function, it does not explain well how a person can move the hand in 3D space to perform activities. Instead of the active ROM in the shoulder and elbow, the volume in which a person can place the hand(s) can be useful. This volume is called the reachable workspace of the arm. The concept of reachable workspace has been used in analyzing mechanical arm supports [12]. The reachable workspace has also been proposed as a parameter to evaluate shoulder pathologies [7, 13]. For the use in a clinical setting, it is important to have a pragmatic approach. The group of Han [13] developed a pragmatic and intuitive approach using a Kinect camera to assess the upper extremity reachable workspace in people with NMD. The reachable workspace parameter offers a numerical expression of the shoulder functions, that is easy to understand by patients and professionals engaged in the clinical evaluation of the upper limb. The reachable workspace can also be shown graphically in an easy-to-interpret way (Figure 1).

Such a pragmatic approach may also be useful to assess how fatiguing repetitive movements are for a person. In case of increasing fatigue, the reachable workspace decreases. Moreover, the reachable workspace is recommended to assess the effect of using a dynamic arm support on the arm movement of persons with NMD. The presence of an arm support may, however, block the view of the camera observing

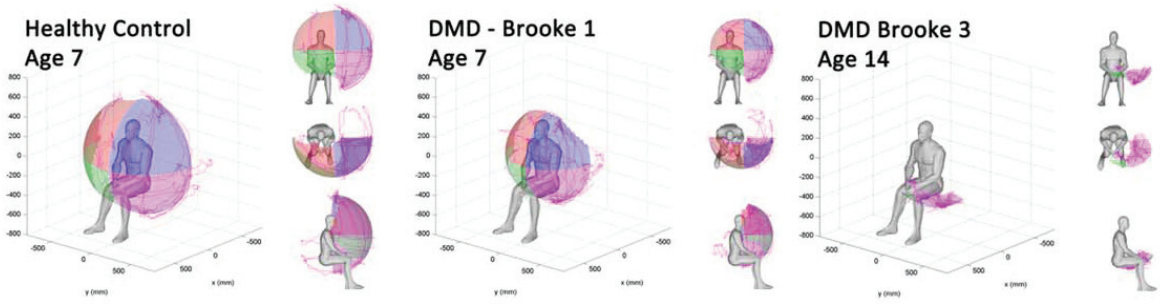

Figure 1: Intuitive graphical visualization of 3D reachable workspace. A 7-year-old, healthy control's reachable workspace viewed from different directions, along with reachable workspaces of individuals with DMD (figure used from Han et al. [13]

the person in the system used by Han. This calls for an alternative way to capture 3D motion data, for example, by using inertial sensors. Such sensors detect forces by sensing linear acceleration along one or several directions (accelerometer), or angular motion about one or several axes (gyroscope) [14].

The CUE and Abilhand questionnaires provided insight in the overall ability of a person to execute certain activities. The CUE and Abilhand questionnaires were useful to explore limitations in people's capacity at a group level. More specific measures to evaluate upper limb capacities during daily activities were, however, lacking when this study started. Recently, the Performance of the Upper Limb (PUL) outcome measure has been developed and validated for the DMD population [15]. Although the instrument has not been validated yet for adults with NMD, it may be a useful instrument for future studies. The actual performance of an individual in his or her current environment is still unknown. Interview-based assessments like the Canadian Occupational Performance Measure (COPM) are recommended to identify during which daily activities individuals perceive limitations, and how satisfied they are about performance of these activities. However, to assess a persons' upper limb performance and related energy expenditure during the day, questionnaires and interviews are not the most appropriate measures. To monitor how a person performs activities, video observation can be used. A disadvantage of video observation is, however, that somebody needs to assess the video material, which makes it a subjective and very time consuming approach. Besides, installing a video system in a patient's home is a problem and involves privacy issues [16]. To determine a person's movement performance during the day, inertial sensors like accelerometers can also be used [17]. The use of accelerometers has been proposed in different research settings

as a reliable and valid assessment of daily physical activity in various populations. Studies have been done for example in healthy children [18], healthy adults [19], young boys with DMD [20] and people with stroke [21]. In most of these studies, accelerometers were attached to the hip and general levels of physical activity of persons were reported. There are, however, also examples where the arm-hand usage in daily life was measured with accelerometers mounted on the wrist [22]. Wrist-worn accelerometers have also been used in clinical studies, for example to estimate the use the affected upper limb of patients with stroke in real-life situations [17, 23, 24] or to quantify characteristics of daily arm activities in patients with COPD [25]. To determine the actual use of the arms during ADL performance, with or without the use of a dynamic arm support, the use of accelerometers is also recommended.

While body movements can be measured with accelerometers, they provide no information on the actual energy expenditure of a person. In a study by Meijer et al. [25], the daily arm activities were assessed using accelerometers in a laboratory environment, while the relative efforts of the trapezius, deltoid and biceps muscles were studied by recording EMG during a set of daily activities. This approach does, however, not provide insight in the actual performance of daily life activities. A combined measurement of physical movement activity and muscle activity is recommended, to estimate how much the arms are moved and how active the muscles are actually used during daily activities. A pilot has been performed to evaluate the feasibility of such a combined recording of accelerations and muscle activity. For this pilot, a six channel mobile system for measuring EMG and accelerations was used (Mobi, TMSi). First, a person was asked to perform a set of simulated daily tasks, while the accelerations of the upper arm were recorded in three directions (x, y and z), while in the meantime the EMG of the trapezius, deltoid, serratus and pectoralis muscles were recorded [26]. Figure 2 shows that tasks that require certain arm movements can be clearly recognized. Figure 3 shows the results of a 4-hour and 9-hour recording, while a person was performing daily activities. Such recordings may be useful to get an objective impression of a person's physical arm activity and how actively the muscles are used.

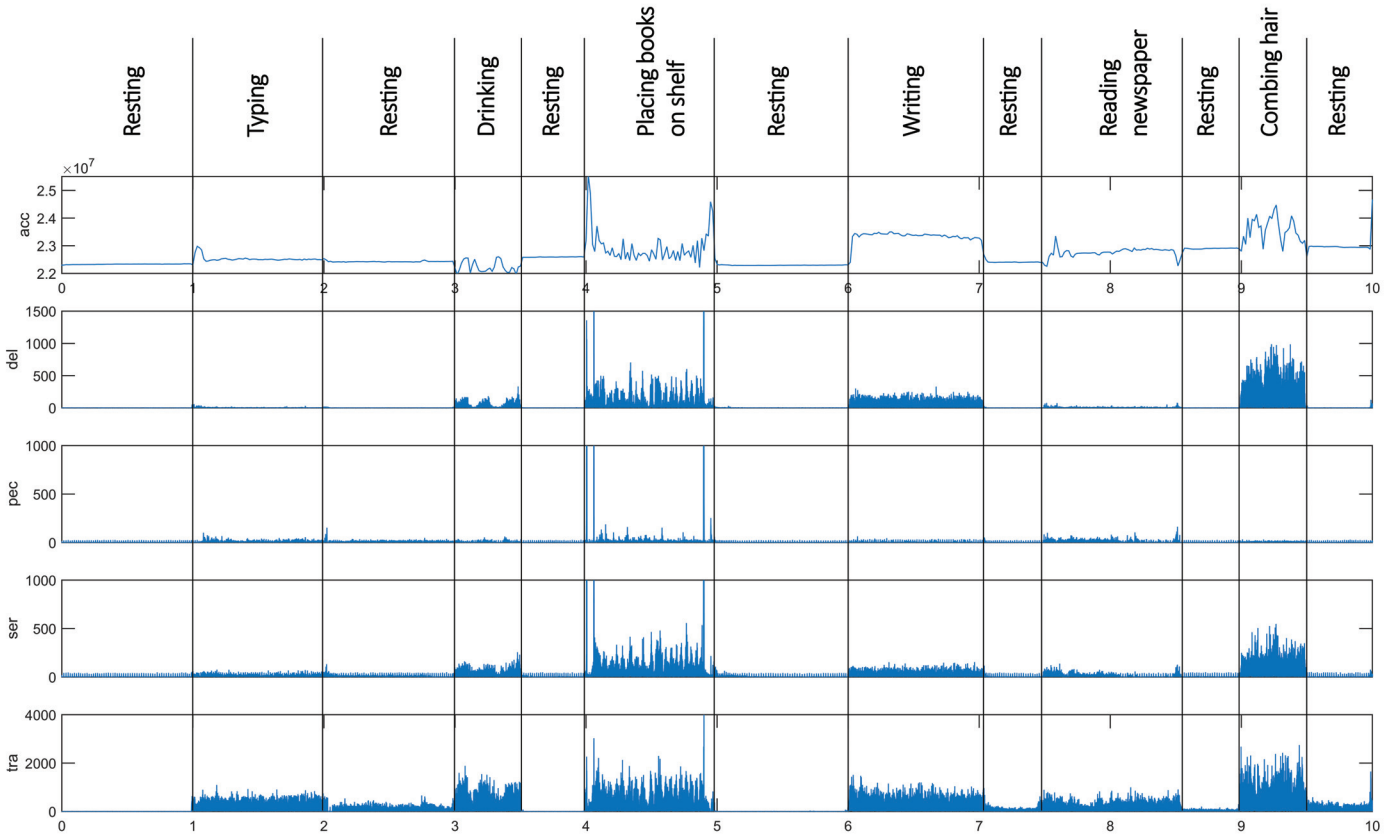

Figure 2: Overview of accelerations of the upper arm and related EMG activity of trapezius, deltoid, pectoralis and serratus muscles during a series of simulated activities performed in a time span of 10 minutes.

While a combined measurement of physical movement activity and muscle activity may be useful to estimate how much the arms are moved during the day, and how active the muscles are actually used during performance of daily activities, such a method is not suitable to look at individual activities that a person is performing. By using motion tracking sensors that include both accelerometers and gyroscopes, also ROM and reachable workspace parameters can be determined over a longer period of time. Such recordings will however generate a huge amount of data that will have little meaning without any contextual knowledge of the activities that are actually performed. It would therefore be beneficial to have an automatic approach to structure the recorded data. A set of tools that was developed to facilitate highly automated, structured recording, analysis and presentation of data is FusionTools, developed by Roessingh Research and Development. This tool uses Hidden Markov Models (HMM), a type of stochastic signal models, that are extensively used in speech classification. The FusionTools have, among other things, been used to classify lifting activities [27]. After a learning period the software can recognize a movement if it is performed in a similar way during training. The feasibility of using such an approach based on Hidden Markov Model techniques to classify arm movements was tested in a group of people with DMD [28]. Five healthy persons and three persons with DMD were asked to perform an alternating series of activities (e.g. eating, drinking, working on a laptop and reaching towards two different points), while arm movements were recorded by using 3D motion tracking sensors (XSens MTx). Although proper calibration was difficult in the persons with DMD who had very limited arm function, activities could be classified successfully [28]. Further development and evaluation of such an approach is recommended in order to evaluate the quality of actual arm-hand performance when an arm support is used.

To summarize, measures on the level of upper limb functions and capacities were studied in this thesis. For future studies, it is recommended to use measures that provide insight in the reachable workspace of the hand and in the performance of upper limb movements during daily life. Figure 4 gives an overview of the specific instruments that are studied and recommended. More insight is needed to have a better understanding of upper limb use in daily life and to develop more individualized treatment interventions like training programs or supportive devices.

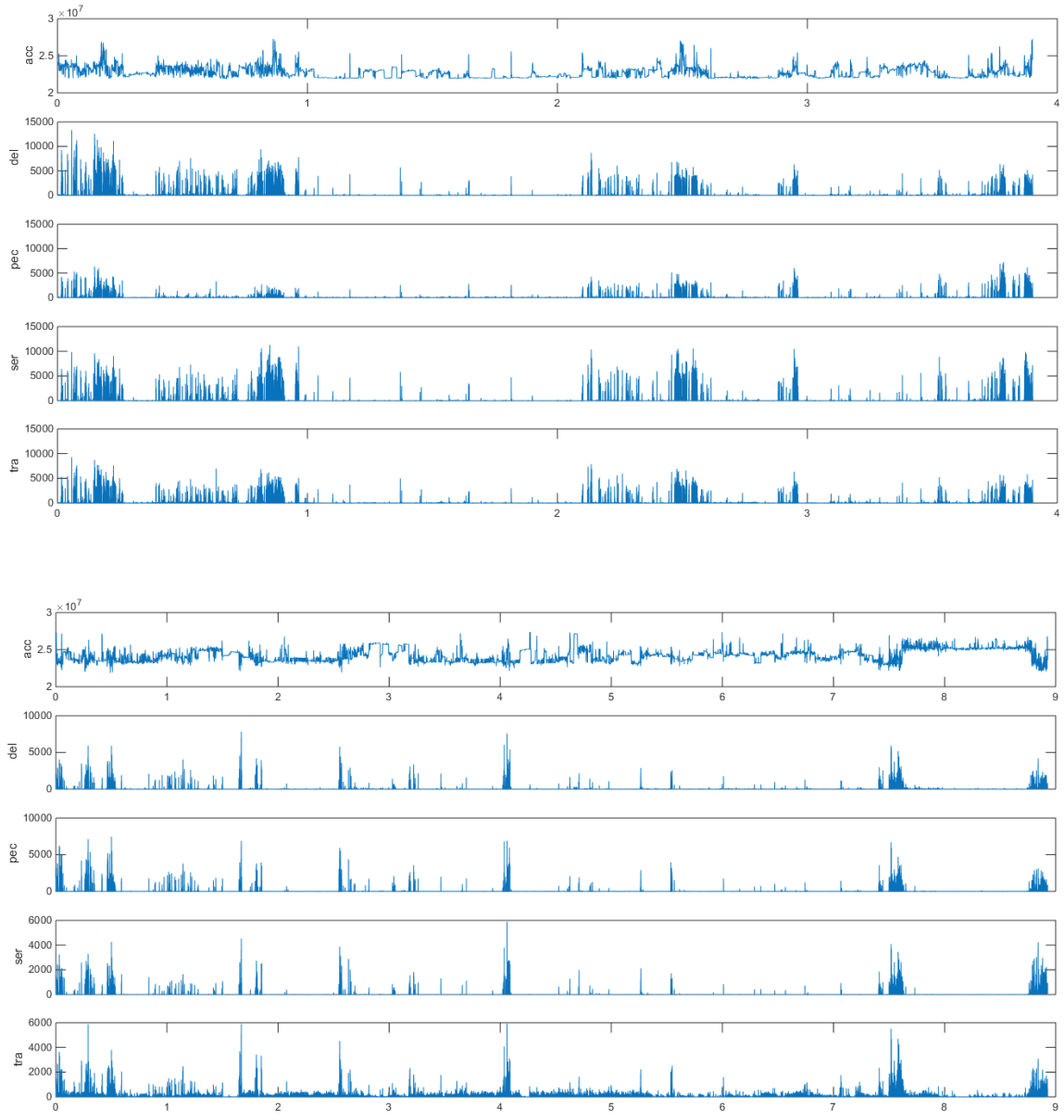

Figure 3: Overview of accelerations of the upper arm and related EMG activity of trapezius, deltoid, pectoralis and serratus muscles, during daily life activities performed in a time span of 4 (left) and 9 (right) hours.

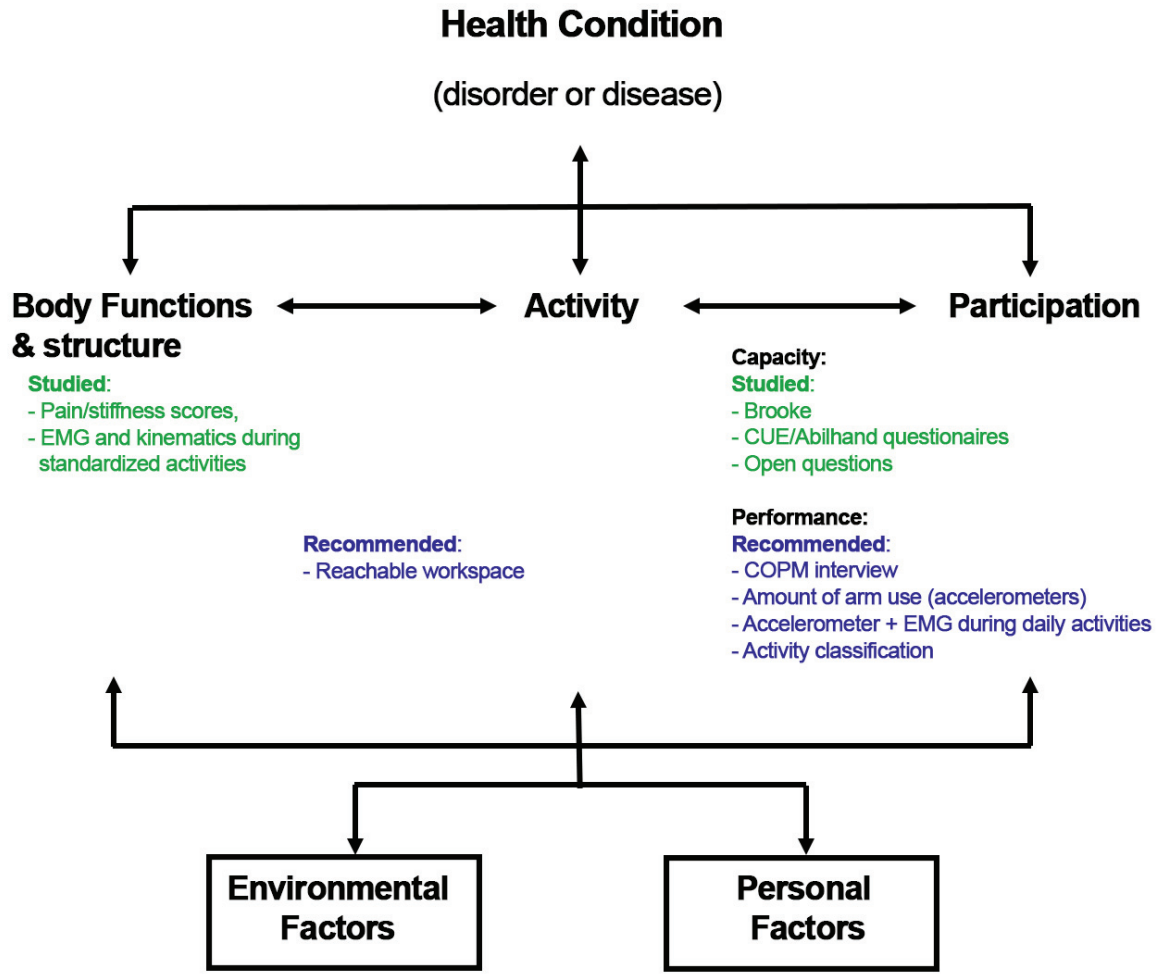

Figure 4: Overview of measures that are studied in this thesis, and measures that are recommended at the different levels of the International Classification of Functioning, Disability and Health (ICF) model (World Health Organization (WHO, 2001)[6]

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Nederlandse samenvatting

9

Armbewegingen spelen een fundamentele rol bij het uitvoeren van dagelijkse activiteiten. Er zijn verschillende neuromusculaire aandoeningen (NMA) die de mogelijkheid om de armen goed te kunnen gebruiken beperken, waardoor de kwaliteit van het leven aangetast kan worden. Ziektebeelden die invloed hebben op het kunnen gebruiken van de armen zijn Facioscapulohumerale dystrofie (FSHD), Limb-girdle spierdystrofie (LGMD), Duchenne spierdystrofie (DMD) en spinale musculaire atrofie (SMA). Om de kwaliteit van leven te verbeteren van mensen met NMA die ernstig beperkt worden in het gebruik van de armen, is het belangrijk om het uitvoeren van dagelijkse activiteiten te vergemakkelijken. Om dit te realiseren kan er bijvoorbeeld gebruik gemaakt worden van hulpmiddelen die de armfunctie vergroten.

Het doel van dit proefschrift is om de functie van de armen te bestuderen bij mensen met verschillende vormen van NMA. Er zijn verschillende benaderingen gebruikt. Er is eerst een literatuurstudie uitgevoerd naar het beloop van de armfunctie, hoe dit wordt gemeten en welke behandelingen er zijn, gevolgd door een vragenlijstonderzoek om de invloed van beperkingen in de bovenste ledematen op het dagelijks functioneren van mensen met FSHD te verkennen. Deze resultaten zijn vergeleken met andere NMA met beperkingen in de armfunctie (LGMD, SMA en DMD) door middel van dezelfde vragenlijsten. Tenslotte is een studie uitgevoerd in het bewegingslaboratorium om bewegingen van de armen in een 3D-omgeving te onderzoeken met en zonder het gebruik van een armondersteuning, en daarnaast is ook naar spieractivatiepatronen gekeken.

Technologie om de bovenste ledematen van mensen met DMD te ondersteunen

Hoofdstuk 2 beschrijft de resultaten van een workshop over de eisen voor armfunctie onderzoek bij mensen met DMD en de techniek die beschikbaar is om de armen te ondersteunen. Deze workshop was specifiek gericht op DMD, omdat er in die groep relatief veel onderzoek is gedaan naar de functie van de armen en het gebruik van hulpmiddelen. De resultaten zijn echter ook relevant voor andere neuromusculaire aandoeningen (NMD). Het primaire doel van de workshop was om mensen uit verschillende disciplines samen te brengen en om te bespreken hoe de ontwikkeling van

nieuwe ondersteunende technologie, die de armfunctie van jonge mannen met DMD kan vergroten, te versnellen. Er waren 24 deelnemers, waaronder ouders, experts op het gebied van gebruikersbehoeften / mens-machine-onderzoek / elektrotechniek / werktuigbouwkunde en clinici die betrokken zijn bij de zorg voor tieners met DMD uit Denemarken, Nederland, het Verenigd Koninkrijk en de Verenigde Staten, die deelnamen aan de workshop. Tijdens de workshop is ingegaan op de behoeften van de gebruikers, de huidige methoden voor de evaluatie van armfunctie, de armsteunen die nu verkrijgbaar zijn, de lopende onderzoeksprojecten om actieve armsteunen te ontwikkelen en opkomende technologieën die nuttig kunnen zijn voor de toekomstige ontwikkeling van ondersteunende technologie voor de DMD doelgroep. Zes clusters van actiepunten werden geïdentificeerd, namelijk (a) het identificeren van gebruiker en verzorger behoeften en hun acceptatie, (b) een beoordeling van de prestaties van de gebruiker en verzorger voor en na het in gebruik nemen van een hulpmiddel, (c) het ontwikkelen van lab en mobiele uitkomstmaten en protocollen, (d) het verzamelen van gegevens over het gebruik van een apparaat, (e) het ontwikkelen van modulaire technologie en (f) het werken aan de toegankelijkheid en de vergoeding in verschillende landen.

Review over de functie en activiteiten van de bovenste ledematen in FSHD en LGMD

Hoofdstuk 3 omvat een literatuurreview over wat er bekend is over het natuurlijke beloop van de functie van de bovenste ledematen en de capaciteit van mensen met FSHD en LGMD om de armen te kunnen gebruiken. Zowel FSHD en LGMD zijn langzaam progressieve ziekten, waarbij de eerste problemen meestal ontstaan op een leeftijd tussen de 10 en 30 jaar oud. Deze studie geeft ook een overzicht van meetinstrumenten die worden gebruikt om de functie van de bovenste ledematen en het uitvoeren van activiteiten bij patiënten met FSHD en LGMD te evalueren. In wetenschappelijke databases (PubMed, MEDLINE, EMBASE, CINAHL en Cochrane) is gezocht naar wat er in de literatuur bekend is over arm- en handfunctie bij mensen met FSHD of LGMD. Deze zoektocht heeft in totaal 247 artikelen opgeleverd, waarvan er uiteindelijk zestien relevant waren voor dit onderzoek. Deze 16 artikelen bevatten informatie over in totaal 272 patiënten met FSHD (gemiddelde leeftijd tussen de 36 en 59 jaar) en 270 patiënten met LGMD (gemiddelde leeftijd van 35 tot 55 jaar). Op basis van deze eerdere onderzoeken is geconcludeerd dat het klinische beeld van

stoornissen betreffende de armfunctie en beperkingen in activiteiten waarin de armen een rol spelen bij mensen met FSHD en LGMD zeer variabel is. Over het algemeen ervaren mensen met FSHD en LGMD problemen met het heffen van hun armen. De uitvoering van taken duurt ook aanzienlijk langer. Het klinische beloop van de functies van de bovenste ledematen en de capaciteiten van mensen met FSHD en LGMD is moeilijk te voorspellen ten gevolge van deze hoge variabiliteit. De meest gebruikte manier om armfunctie te testen is manueel spieronderzoek. In de review die is gedaan was het niet mogelijk om de resultaten van deze spieronderzoeken te vergelijken tussen de verschillende studies, omdat in de meeste studies alleen een samengestelde score van verschillende spiergroepen is beschreven in plaats van scores voor de individuele spiergroepen. Hoewel manueel spieronderzoek beschouwd wordt als een goede methode om het verloop van een ziekte te beschrijven, is het geen betrouwbare methode om spierkracht kwantitatief te meten. Er is een studie gevonden waarbij de onderzoekers gebruik gemaakt hebben van elektromyografie (EMG) van verschillende spieren (biceps brachii, brachioradialis, triceps en deltoideus anterior) tijdens een gesimuleerde drinktaak. De onderzoekers die dit onderzoek gedaan hebben, ontdekten dat de gemeten EMG-activiteit tijdens deze taak hoger was bij mensen met FSHD dan bij gezonde personen. De spieractiviteit en het bewegingspatroon bij de FSHD groep omvatte meer synergistische spieractiviteit en meer abductie en flexie in de schouder- en ellebooggewrichten. Om te evalueren in hoeverre mensen in staat zijn de armen te gebruiken tijdens activiteiten, wordt de Brooke schaal (score van 1 tot 6, 1=volledige arm en handfunctie, 6=geen nuttige arm en handfunctie) het meest gebruikt. Mensen met FSHD melden echter niet vaak een score van 5 of 6, waardoor de Brooke schaal niet gevoelig is voor het meten van kleine verschillen in de capaciteit van de bovenste ledematen. Daarnaast classificeert de Brooke schaal alleen de capaciteit van basale reiktaken. Meer specifieke instrumenten om de capaciteit van de bovenste ledematen en de prestaties tijdens dagelijkse activiteiten te evalueren werden vrijwel niet gebruikt. Hoewel methoden als manueel spieronderzoek en de Brooke schaal veel gebruikt worden, is er een gebrek aan meer specifieke uitkomstmaten om de functie, capaciteit en de prestaties van de bovenste ledematen te beoordelen. Op basis van de review zijn andere instrumenten aanbevolen, zoals 3D bewegingsanalyses en EMG (spieractiviteit) opnames, om meer inzicht te krijgen in de functie van de bovenste ledematen. Daarnaast worden vragenlijsten zoals de Abilhand aangeraden om de capaciteit van de bovenste ledematen te kunnen beoordelen, en is het gebruik van accelerometers voorgesteld om prestaties in het dagelijks leven te kunnen evalueren.

Bovenste ledematen functie en de activiteit in FSHD

In **hoofdstuk 4** zijn de armen bij mensen met FSHD onderzocht op de niveaus van stoornissen in functie, beperkingen in activiteiten en restricties in participatie van de 'International Classification of Functioning Disability and Health' (ICF). Er is een online enquête ontworpen, met uitkomstmaten op alle drie deze niveaus van de ICF. De enquête bevat vragen over pijn en stijfheid, de Brooke schaal, een vragenlijst om de mogelijkheden van de bovenste ledematen te evalueren (CUE), een vragenlijst om de moeilijkheid van het uitvoeren van bepaalde activiteiten in kaart te brengen (Abilhand-plus) en open vragen met betrekking tot sociale participatie. Achtentachtig mensen met FSHD hebben de vragen beantwoord. Naast het bekende probleem van mensen met FSHD om de armen te heffen boven schouderhoogte, is uit de enquête ook gebleken dat activiteiten waarbij de armen niet hoog opgetild hoeven te worden ook problematisch zijn bij patiënten met FSHD. Meer dan 40% van de respondenten met FSHD hebben aangegeven pijn te ervaren in één of beide armen. De resultaten hebben aangetoond dat hogere pijn en stijfheid scores en een langere ziekteduur geassocieerd zijn met een verhoogde beperking in het uitvoeren van activiteiten. Ongeveer 80% van de respondenten heeft aangegeven beperkingen te ervaren bij werk gerelateerde activiteiten, tijdens het deelnemen aan sport activiteiten, het uitvoeren van hobby's, huishoudelijke activiteiten en in intieme relaties.

Bovenste ledematen kinematica en spieractivatiepatronen bij mensen met FSHD

Mensen met FSHD hebben een verhoogd risico op pees- of spierschade door het maken van compenserende bewegingen die vaak gebruikt worden om de armen te heffen en om het gebrek aan spierkracht rond het schouderblad te compenseren. Innovatieve armsteunen kunnen mensen met FSHD helpen bij het uitvoeren van activiteiten die veel moeite kosten of die mogelijk schade kunnen veroorzaken. Om dit soort apparaten te optimaliseren en om de effectiviteit ervan te evalueren, zijn kwantitatieve en objectieve evaluatiemethoden nodig. Kwantitatieve gegevens zijn bijvoorbeeld parameters zoals het bewegingsbereik van armbewegingen en de hoogte van de spieractiviteit tijdens het bewegen van de armen. Een eerder onderzoek van Bakhtiary et al. heeft een eerste indruk gegeven van deze parameters tijdens het

uitvoeren van een gesimuleerde drink taak. In dat onderzoek is echter niet gekeken naar spieren die verantwoordelijk zijn voor het stabiliseren van het schouderblad. **Hoofdstuk 5** beschrijft de kinematica van de bovenste ledematen en de betrokkenheid van een aantal specifieke spieren (biceps brachii, deltoideus, triceps brachii, trapezius (bovenste deel), grote borstspier (claviculaire deel) en de brede rugspier) van mensen met FSHD en gezonde personen tijdens het uitvoeren van verschillende soorten taken. Elf mensen met FSHD en acht gezonde vrijwilligers hebben aan deze studie deelgenomen. Deelnemers werden gevraagd om een set van zes gestandaardiseerde bewegingen (schouderabductie-adductie, schouder flexie-extensie, reiken naar beide kanten op schouderhoogte, het verplaatsen van de hand naar de mond en het duwen-trekken van een voorwerp op een tafel) uit te voeren. Voor elke persoon en iedere taak is vervolgens bepaald wat de maximale hoek was tussen de romp en de bovenarm (geeft aan hoe hoog mensen de bovenarm konden heffen) en wat de minimale en maximale hoek in de elleboog was. We hebben kinematische verschillen gevonden tussen de FSHD groep en de gezonde controlegroep, vooral in de hoogte van de schouder elevatiehoek. Slechts één persoon met FSHD was in staat om de arm boven 120º te heffen tijdens de schouder abductie-adductie en flexie-extensie bewegingen. In vergelijking met gezonde personen is in de personen met FSHD tijdens het uitvoeren van de bewegingen waarbij de bovenarm geheven moest worden meer spieractiviteit gemeten. De activiteit van de trapezius was tijdens een aantal bewegingen zelfs bijna net zo hoog als de spieractiviteit die gemeten was tijdens een beweging waarbij mensen gevraagd werd de spieren maximaal aan te spannen. Ook de deltoïdeus en pectoralis spieren waren zeer actief. Er is geconcludeerd dat de hogere activatie van de trapezius bij patiënten met FSHD duiden op een mechanisme om de zwakke schouderspieren te ondersteunen tijdens het heffen van de armen op schouderhoogte.

Effect van onderarm zwaartekrachtcompensatie op de kinematica en spieractiviteit in de bovenste ledematen bij mensen met FSHD

Armondersteuningen zijn ontwikkeld ter compensatie van het verlies van armfunctie. In **hoofdstuk 6** wordt het effect gemeten van het compenseren van de zwaartekracht op de kinematica en spieractiviteit van de armen van mensen met FSHD en gezonde personen. Dit is gedaan terwijl mensen een aantal gestandaardiseerde armtaken

(schouderabductie-adductie, schouder flexie- extensie, reiken naar beide kanten op schouderhoogte, bewegen van de hand naar de mond en het duwen-trekken van een voorwerp op een tafel) uitvoerden. Aan elf mensen met FSHD (Brooke score 2-3) en acht gezonde vrijwilligers is gevraagd om een set van bewegingen uit te voeren, eerst met en daarna zonder de hulp van een arm ondersteuning die de onderarm ondersteunde (SLING armsteun). Veranderingen in de schouder kinematica en spieractiviteit werden gekwantificeerd, terwijl de deelnemers een set van gestandaardiseerde taken uitvoerden met en zonder de SLING onderarmsteun. De gezonde vrijwilligers konden met de armsteun de armen minder hoog optillen als gevolg van het mechanische ontwerp van de armsteun. Dit verschil werd niet waargenomen bij mensen met FSHD, omdat ze de armen niet zo hoog konden optillen dat ze hier last van hadden. Er is in beide groepen ook aangetoond dat er minder spieractiviteit nodig was om activiteiten uit te voeren met armsteun in vergelijking met activiteiten die zonder armsteun uitgevoerd werden. Het bewegen van de hand naar de mond en het maken van rechte schouderbewegingen (abductie-adductie, flexie-extensie) ging sneller wanneer de SLING werd gebruikt. Reiken en het duwen-trekken van een object op tafel ging daarentegen langzamer met de SLING. De hoeveelheid rompbewegingen werd in zowel de FSHD groep als in de controle groep minder tijdens de SLING ondersteunde schouderbewegingen. Zoals verwacht zorgde het ondersteunen van de armen tijdens alle bewegingen in alle spieren voor een vermindering van de spieractiviteit, wat ook de resultaten uit eerdere onderzoeken met gezonde proefpersonen bevestigen. Het gebruiken van de SLING resulteerde in het later aanspannen van de biceps en deltoideus-spier tijdens beide reiktaken in de FSHD groep. Daarnaast werd ook een latere aanspanning van de trapezius spier gevonden tijdens de reiktaak naar de andere kant (met de rechterhand naar links reiken) in de FSHD groep. Deze bevinding impliceert dat de FSHD groep het zwaartekracht compensatie mechanisme meer in hun voordeel konden gebruiken wanneer stabiliteit van het schouderblad nodig was. Om het profiel van armsteun gebruikers nog beter te begrijpen, moet de informatie over de spieractiviteit worden aangevuld met informatie over momenten en krachten in de gewrichten. Daarnaast is het van belang dat dan ook gekeken wordt naar andere spieren die het schouderblad stabiliseren, zoals het onderste deel van de trapezius en de serratus anterior.

Verschillende profielen van de bovenste ledematen functie in vier soorten NMD

De vragenlijst die naar de FSHD groep is gestuurd (hoofdstuk 4), is ook voorgelegd aan een groep mensen met DMD, LGMD en SMA. In **hoofdstuk 7** zijn de stoornissen, beperkingen in activiteiten en restricties in sociale participatie met betrekking tot de armen die gemeld zijn door mensen met FSHD vergeleken met die van mensen met LGMD, SMA en DMD in Nederland. Het doel van deze studie was om te onderzoeken of verschillende profielen van de functie van de armen geïdentificeerd kunnen worden tussen verschillende vormen van neuromusculaire aandoeningen (NMA). Op het niveau van de armfunctie van de zijn vragen gesteld over pijn en stijfheid in de armen, handen en vingers. Om de capaciteit van het gebruik van de armen tijdens basisactiviteiten te beoordelen, zijn de Brooke schaal en de CUE vragenlijst (mogelijkheden van de bovenste ledematen) gebruikt. De Abilhand-plus vragenlijst is gebruikt om de capaciteit van het kunnen uitvoeren van dagelijkse activiteiten te evalueren. Tot slot zijn er een aantal open vragen gesteld met betrekking tot sociale participatie. In totaal hebben 267 mensen deelgenomen aan de studie (FSHD = 88, LGMD = 65, SMA = 64, DMD = 50), waarvan 222 mensen de complete vragenlijst ingevuld hebben. De gemiddelde leeftijd van de DMD-groep was 15 jaar. In de SMA, LGMD en FSHD groepen varieerde de gemiddelde leeftijd tussen de 39 en 51 jaar. In de FSHD en LGMD groepen was minder dan 23% van de respondenten volledig rolstoel gebonden, terwijl dit in de SMA en DMD groepen meer dan 64% was. Het gebruik van armsteunen was het hoogst in de SMA-groep (28,1%) en het laagst in de LGMD groep (11,5%). Wanneer alleen gekeken werd naar de mensen die mogelijk zouden kunnen profiteren van een armsteun (Brooke scores 2-6), werd het gebruik van een armsteun gemeld door respectievelijk 19,4%, 20,3%, 36,7% en 27,8% van de mensen met FSHD, LGMD, SMA en DMD. De gemiddelde Brooke score was het hoogst in de DMD-groep en het laagst in de LGMD groep. Pijn in een of meer segmenten van de bovenste ledematen werd gerapporteerd door meer dan 30% van de respondenten. De hoogste frequenties van pijn werden gemeld door mensen met FSHD in de schouder en bovenarm. De gerapporteerde pijnscores waren sterk gerelateerd aan de gerapporteerde stijfheidscores, en er is gesuggereerd dat pijn en stijfheid niet altijd gemakkelijk te onderscheiden zijn van elkaar als subjectieve gevoelens. De meeste beperkingen in het uitvoeren van activiteiten met de armen werden gemeld door personen met DMD en SMA. In deze twee groepen werd aangegeven dat respectievelijk 37% en 24% van de ABILHAND-

plus activiteiten onmogelijk uit te voeren waren, en dat respectievelijk 32% en 26% van deze activiteiten moeilijk zijn om uit te voeren. In FSHD en LGMD werd slechts van respectievelijk 2% en 5% van de ABILHAND-plus activiteiten gemeld dat deze onmogelijk uit te voeren waren, en dat respectievelijk 26% en 17% van de activiteiten moeilijk uit te voeren waren. Net zoals gemeld werd door mensen met FSHD, melden ook mensen met LGMD relatief hoge scores voor pijn en stijfheid en lage scores voor beperkingen in het kunnen uitvoeren van activiteiten. Het profiel van de DMD en SMA groep daarentegen werd gekenmerkt door relatief lage scores voor pijn en stijfheid en hoge scores voor beperkingen in activiteiten. Deze resultaten geven aan dat er binnen de verschillende soorten NMA verschillende profielen van armfunctie bestaan. Terwijl het profiel dat bij personen met FSHD en LGMD waargenomen werd eerder duidt op overbelasting, is bij mensen met DMD en SMA juist sprake van verminderd gebruik van de bovenste ledematen. Er is gesuggereerd dat beide patronen een andere revalidatie strategie vereisen.

Discussie

In dit proefschrift is de armfunctie onderzocht bij mensen met verschillende neuromusculaire aandoeningen (NMA). Dit is onder andere gedaan door onderzoek van kinematica en spieractiviteit tijdens het uitvoeren van verschillende activiteiten. Deze onderzoeken hebben geholpen om inzicht te krijgen in de toegevoegde waarde van een armondersteuning op het niveau van de activiteit van spieren en het bewegingsbereik in de schouder en elleboog bij mensen met FSHD. Er is ook gekeken naar pijn en stijfheid die mensen ervaren in de schouders, armen en handen. Tot slot is de capaciteit om activiteiten met de armen uit te kunnen voeren bekeken door middel van de Brooke score, de CUE- en ABILHAND-plus vragenlijst en een aantal open vragen. Deze instrumenten hebben een tweetal profielen opgeleverd (overbelasting en verminderd gebruik) tussen verschillende typen NMA. Hoewel deze onderzoeken bij hebben gedragen aan een beter inzicht op het niveau van de functie van de armen en de beperkingen in het uitvoeren van bewegingen, is het nog onbekend hoe mensen daadwerkelijk presteren tijdens het uitvoeren van dagelijkse activiteiten. Om te achterhalen welke beperkingen individuele mensen met NMA ervaren bij de uitvoering van de dagelijkse activiteiten, en hoe zij deze activiteiten scoren op belangrijkheid, uitvoering en tevredenheid wordt naast het gebruik van gestandaardiseerde vragenlijsten het gebruik van een cliëntgerichte maat aanbevolen zoals de Canadian Occupational

Performance Measure (COPM). Daarnaast is het nog onbekend hoe mensen daadwerkelijk presteren tijdens het uitvoeren van dagelijkse activiteiten, met en zonder het gebruik van een armondersteuning. Om dit in kaart te kunnen brengen zijn de volgende aanbevelingen gedaan:

- Meten van het totale bewegingsbereik van de hand met behulp van een methode die zowel met als zonder armondersteuning gebruikt kan worden (bijv. met inertiele sensoren).
- Kwantificeren hoeveel de armen daadwerkelijk gebruikt worden tijdens het uitvoeren van dagelijkse activiteiten, met of zonder het gebruik van een armondersteuning (bijv. met accelerometers).
- Inzicht krijgen in de mate waarin de spieren gebruikt worden gedurende de dag, door het meten van de activiteit van bepaalde spieren met een mobiel EMG meetsysteem.
- Verder ontwikkelen en evalueren van methoden om grote hoeveelheden bewegingsdata te classificeren, om niet alleen een globaal inzicht te krijgen in het gebruik van de armen, maar om ook specifieke activiteiten zoals bijvoorbeeld eten of drinken te kunnen bestuderen.

Appendices

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Curriculum vitae

Arjen Bergsma was born in Donkerbroek on February 10th, 1984. After graduating from secondary school (CSG Liudger in Drachten), he started studying Biomedical Engineering at the University of Twente. During an internship at the Roessingh rehabilitation center in 2008, he became interested in technology for people with mobility problems. For his master thesis, he investigated how arm functions of people with severe muscular dystrophy can be supported. Arjen graduated in 2009. As a direct result of his masters project, the Flextension Foundation was founded, with the aim to stimulate development of new supportive technology to improve quality of life of people with Duchenne (Arjen is involved as board member). In 2009, Arjen started working as freelance biomedical engineer, and he had various research groups as contractors. He coordinated among others the grant application process (STW) of the Flextension A-Gear project. In 2011, he started a part-time PhD research at the Department of Rehabilitation at the Radboudumc under supervision of dr. Imelda de Groot and dr. Edith Cup. He also collaborated closely with the Department of Movement Sciences at the Maastricht University Medical Centre under supervision of dr. Kenneth Meijer. In relation to his PhD activities, he participated in 2013 in the Radboud Da Vinci Challenge, a program that offers excellent PhD students and post-docs the opportunity to experience broad personal development. In 2014, Arjen was involved in initiating the Symbionics program (STW Perspectief) and the eNHANCE project (Horizon2020), with the aim to develop sophisticated assistive technology that adapts to the users' needs. Both proposals were successfully granted in 2014, and Arjen became involved in both projects as coordinator. Arjen is also interested in rehabilitation technology across borders. In 2010 he volunteered in the $50 prosthesis project of the Waag Society in Amsterdam, and in 2011 he did a four-weeks field study into low-cost prosthetics in the area of Yogyakarta, Indonesia. He also co-founded the MoveAid Foundation, with the goal to improve prosthetic solutions adapted to the needs of people with an amputation living in developing countries. In 2014, MoveAid joined forces with the Movendi Foundation, where Arjen became one of the board members. In 2015, he was involved in the start of the Community of Prosthetics Practice (CoPP), which falls under the umbrella of the GATE initiative of the WHO. Aim of the CoPP is to develop and provide a holistic approach to prosthetic rehabilitation and service delivery for people with lower limb amputations who live in rural areas.

Arjen has an entrepreneurial spirit and he likes to support others with converting ideas into concrete projects. Arjen is very interested in people and rehabilitation technology. His passion is to bring experts from different disciplines together to jointly develop new solutions. Arjen resides with Sophie Schipper in Utrecht. He likes to be in the sky to fly as private pilot, and together with Sophie he likes to travel around the world.

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